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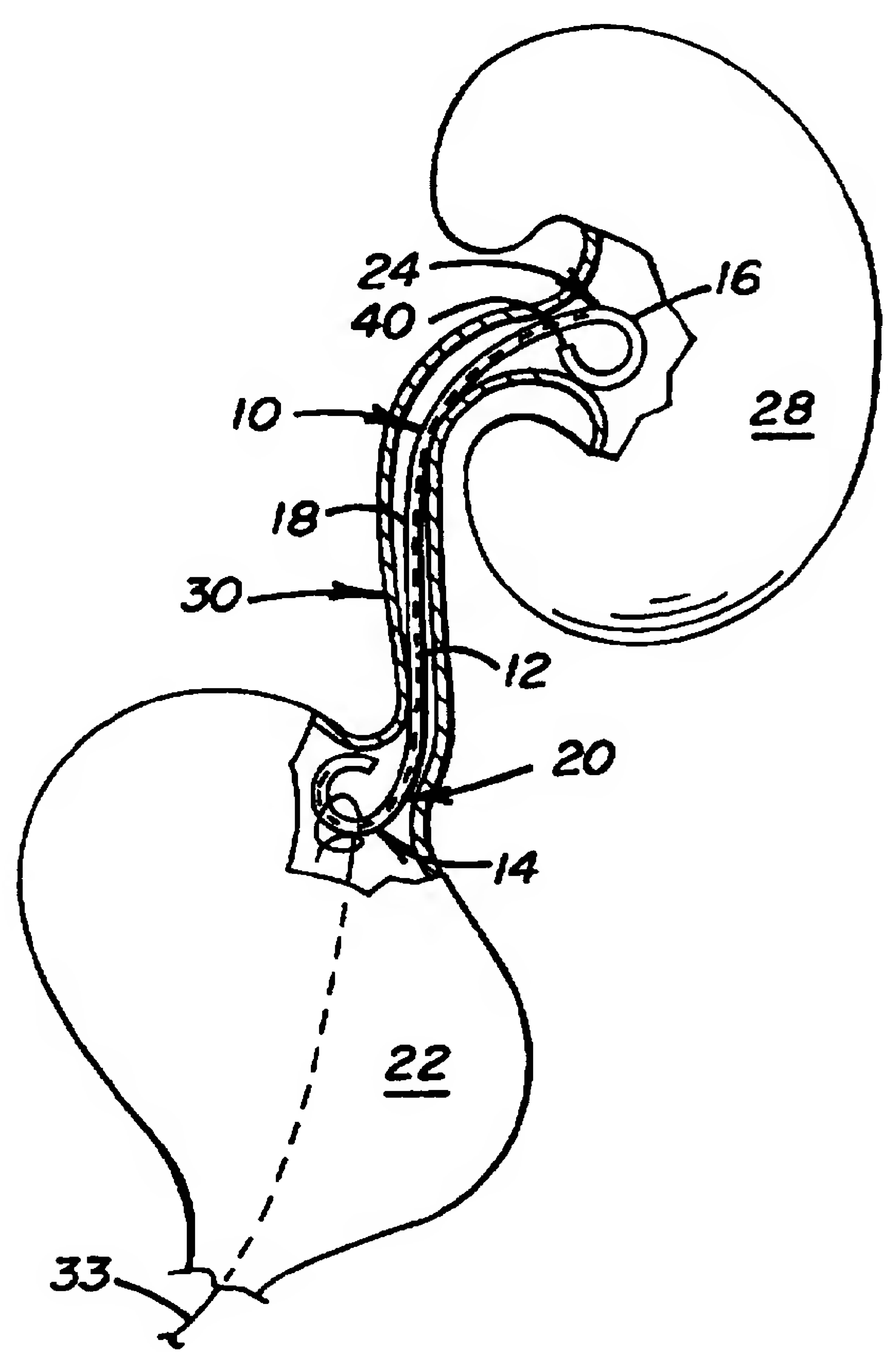
(57) Abstract

In accordance with the invention, there are provided medical devices with incorporated shape memory systems that allow a polymeric medical device to be inserted in a first conformation or configuration and revert to a second conformation or configuration. In another aspect of the invention, there is provided a medical device, such as a ureteral stent that comprises an elongate member (10) having a proximal end portion and a distal end portion joined by a body portion. The elongated member has an initial outer diameter. The member is formulated of a physiologically acceptable polymer capable of hydrating and expanding.



POLYMERIC MEDICAL DEVICE SYSTEMS HAVING SHAPE MEMORY

DESCRIPTION

CROSS-REFERENCE TO RELATED APPLICATION

The present application is a continuation-in-part application of U.S. Patent Application, Serial No. 08/000,274, filed January 4, 1993, the disclosure of which is hereby incorporated herein by reference in its entirety.

TECHNICAL FIELD

The present invention relates to implantable or insertable medical devices. More specifically, it relates to implantable or insertable medical devices comprising a physiologically acceptable polymer which upon hydration, a change in temperature, and/or a combination thereof, is capable of expanding and softening or to change shape to a predetermined degree and in a predetermined manner, for example, upon implantation in or insertion into a patient. In certain embodiments, for example, stents can be conformed into a first configuration for easy insertion and following insertion can revert into a second configuration for better retention.

BACKGROUND OF THE INVENTION

Stents are used in a variety of medical procedures. For example, stents are often used in connection with assisting drainage from the kidney through the ureter, from the liver through the biliary ducts, from the gall bladder through the cystic, hepatic, or common bile ducts, dorsal or ventral pancreas through the pancreatic ducts, and the like. A leading reason for stent deployment in ducts is to provide drainage to circumvent a blockage. Blockage of ducts in the body can be a serious and very painful affliction that can result in death if not promptly and effectively treated. Blockages can occur for a number of reasons.

For example, in the kidney and gall bladder, stones, or debris from such stones, can pass into the ureter or the bile ducts where they become entrapped. Alternatively, cysts or tumors growing against the outer wall of the ducts can cause constriction of the ducts. Similarly, internal or duct wall cysts or tumors can act to block ducts.

In many cases, the problem is solved by surgery, medication, or waiting until debris is naturally cleared from the duct. However, a stent must often be inserted in the duct on at least a temporary basis to provide drainage until the condition can be corrected.

Similarly, blood vessel stents are often used in grafting and supporting blood vessel tissues following invasive medical procedures, such as vascular surgery and angioplasty. Similar concerns are also raised in the catheter and intubation arts, in general, which include, without limitation: intravenous catheters, guiding catheters, sheaths, umbilical catheters, trocar catheters, heart catheters including, valvostomy catheters, angioplasty catheters, arthroscopy catheters, and the like), perfusion catheters, suction catheters, oxygen catheters, endoscopy catheters, endotracheal tubes, stomach tubes, feeding tubes, lavage tubes, rectal tubes, urological tubes, irrigation tubes, aneurysm shunts, stenosis dialators, trocars, and inserters.

Looking in particular at ureteral stents by way of example, there are many different stents available. The main function of each of these ureteral stents is to bypass ureteral obstruction and to provide urinary drainage from the kidney to the bladder for a period of time which varies but is usually of the order of a few days to several months.

There are several methods of stent placement within the ureter. One method involves passing a guide wire up the ureter into the kidney. Thereafter, a tubular stent is fed and coaxially slid up the guide wire into the ureter using a tubular stent pusher. An alternate method employs placing a tubular stent having a closed or partially tapered shut proximal end over a guide wire. The stent is thereafter advanced up into the ureter by pushing the guide wire against the

closed or partially tapered shut end. Another alternate method is to place the tubular stent over the guide wire with the stent pusher over and affixed to the guide wire behind the stent and thereafter to advance the entire assemblage into the ureter. These methods can also be used, with appropriate surgery to provide access, to insert a stent from the kidney downwardly through the ureter to the bladder.

Early ureteral stents were straight. As a result, after placement into the ureter, these straight stents often migrated or were expelled from the ureter as a result of peristaltic action by the ureter. Later ureteral stents, therefore, were usually designed with means of retention on one or both ends of the stent. The retention means is intended to inhibit stent migration either upward into the kidney or downward into the bladder. Retention means that have been employed are in the form of hooks, pigtails, coils, corkscrews, malecots, barbs, mushrooms, or any other practical shape that will serve the purpose.

Ureteral stents also come in many different lengths. The variations in stent length are often necessary to accommodate the different ureter lengths in different size patients. As a result, a stock of different length ureteral stents must often be kept available. To overcome this problem of stocking many different length ureteral stents, some stents have been designed in the form of an expanding coil or corkscrew as disclosed in U.S. Patent Nos. 4,531,933; 4,643,716; 4,671,795; and 4,813,925, or utilize connectors as disclosed in U.S. Patent No. 4,790,810.

In addition to varying lengths, ureteral stents are also made with varying diameters, e.g., from 3 French (1 mm) to 16 French (5.28 mm), and typically, 4.5 French (1.5 mm) to 8.5 French (2.8 mm), and varying degrees of hardness. Ureteral stents with smaller diameters are usually easier to insert but may not provide sufficient drainage, whereas stents with larger diameters allow for increasing drainage capacity through the ureter but may be difficult to insert. Stiff ureteral stents are also easier to insert than are softer stents, but once inserted can lead to increased patient discomfort. Softer stents, on the other

hand, provide more comfort for the patient but are more difficult to insert due to their softness. Presently, most available stents are either made of silicone as disclosed in U.S. Patent No. 4,212,304 or of a harder polymer. Silicone may increase patient comfort, but because of the softness of silicone, it is more difficult to guide the stent into the ureter. Once in the ureter, the softness of the silicone increases the likelihood of migration of the stent because rigid retention means are not available.

To balance ease of insertion, better retention and patient comfort, some ureteral stents have been designed combining a stiff material at the kidney end for easier insertion and better retention with a softer material at the bladder end for patient comfort. These dual hardness stents are disclosed in U.S. Patent Nos. 4,820,262; 4,874,360; and 4,931,037.

It is at times desirable or necessary to provide a stent which is wider at one end, either its proximal end or its distal end, perhaps as much as 16 French in diameter, and narrower at the other end, perhaps 4.5 French to 7 French. In the past, this has usually required insertion from the proximal (kidney) end of the ureter, a relatively difficult procedure.

Swellable ureteral stents utilizing hydrophilic polymers of the nature set forth in U.S. Patent 4,377,010 and elsewhere, generally as coatings on other materials but also alone, have been investigated using piglets (See <u>An Experimental Study of Hydrophilic Plastics for Urological Use</u>, J.W.A. Ramsey, et al, British Journal of Urology, <u>Volume 58</u>, pp 70-74, 1986 and/or <u>Evaluation of Polymeric Materials for Endourologic Devices</u>, H.K. Mardis, Seminars in Interventional Radiology, <u>Volume 4, Number 1</u>, pp 36-45, March 1987) but have not received acceptance in the medical community. Such stents have not been formulated with different softnesses and/or swellabilities at different portions thereof whereby optimal comfort combined with retainability, ease of insertion and the ability to provide stents which will assume specially desired shapes on hydrating have not been available or contemplated.

Similar problems described above in respect of ureteral stents exist in the

art of stents in general. Indeed, many of the aforementioned problems are common to a variety of medical devices that are inserted or implanted in a patient.

Certain work has been done in shape memory technology. For example, certain shape memory metals exist, such as Nitinol. Shape memory has been simulated using certain hydrophilic polymers, i.e., in the context of softening and expanding materials. Mardis, *supra*. Recently, in U.S. Patent No. 5,234,457 to Anderson, a type of shape memory was used in intravenous stents. There, a metallic mesh stent was compressed and impregnated with a softenible material, such as a gelatin or a resorbable polymer. The stent, upon softening of the softenible material, would expand against the artery or vein.

Thus, although stents and medical devices have been designed to address one or more of the above problems specifically, there are currently no devices incorporating features that can be used to bypass most of the aforementioned disadvantages. It would thus be desirable to have a medical device that provides one or more of the following attributes, easy insertion or implantation, selectable and different degrees of softening and/or swelling on different portions of the stent, a tapered tip that expands to an adequately large size once expanded, strong retention, insertable or implantable into a small space yet can, if desired, assume a different configuration, size, or shape (i.e., such as a significantly larger diameter at the distal and/or the proximal end upon hydration or another retention means), and, at the same time, increases patient comfort.

DISCLOSURE OF INVENTION

The present invention is directed to overcoming one or more of the problems as set forth above.

In accordance with a first aspect of the present invention, there is provided a polymeric medical device designed for internal use in a patient, comprising a polymer structure that would ordinarily assume a first conformation and a hydrophilic polymer coated upon at least a portion of the structure, the hydrophilic polymer being in a second conformation and having sufficient rigidity whereby the polymer structure is held in the second conformation, wherein upon hydration of the hydrophilic polymer the polymer structure assumes the first conformation. In a preferred embodiment, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%. In another preferred embodiment, the polymer structure comprises an interpenetrating network.

In accordance with a second aspect of the present invention, there is provided a polymeric medical device designed for internal use in a patient, comprising a polymer structure, the polymer structure comprising a first polymer material preconfigured into a first conformation and a second hydrophilic polymer material preconfigured into a second conformation, the first and second polymers having respective mechanical strengths, the mechanical strength of the second polymer material exceeding that of the first polymer material sufficiently so that the polymer structure is in the second conformation, wherein the second polymer material is adapted to lose its mechanical strength upon the occurrence

of a triggering event and upon loss of the mechanical strength of the second polymer, the device assumes the first conformation.

In a preferred embodiment, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the triggering event is an increase in temperature. Or, alternatively, the triggering event is hydration of the second polymer material. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%. In another preferred embodiment, the first polymer comprises an interpenetrating network. In still another preferred embodiment, the polymer structure comprises an interpenetrating network.

In accordance with a third aspect of the present invention, there is provided a method to manufacture a polymeric structure having shape memory properties, comprising: providing a polymeric structure comprising a first polymer formed into a first conformation; applying a hydrophilic polymer to at least a portion of a surface of the polymeric structure; deforming the polymeric structure from the first conformation into a second conformation under conditions designed to permit the polymeric structure to retain a memory of the first conformation; and allowing the hydrophilic polymer to harden and hold the polymeric structure in the second conformation.

In a preferred embodiment, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl

cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

In accordance with a fourth aspect of the present invention, there is provided a method to manufacture a polymeric structure having shape memory properties, comprising: providing a polymeric structure comprising a first polymer and a second polymer formed into a first conformation, the first and second polymers having respective mechanical strengths, the second polymer being capable of losing its mechanical strength upon the occurrence of a triggering event; and deforming the polymeric structure from the first conformation into a second conformation under conditions designed to permit the polymeric structure to retain the memory of the first conformation and to permit the mechanical strength of the second polymer to hold the polymeric structure in the second conformation.

In a preferred embodiment, the second polymer is a hydrophilic polymer. Preferably, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the triggering event is an increase in temperature. Or, alternatively, the triggering event is hydration of the second polymer material. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

In accordance with a fifth aspect of the present invention, there is provided a medical device designed for internal use in a patient, comprising a structure that would ordinarily assume a first conformation and a hydrophilic

polymer coated upon at least a portion of the structure, the hydrophilic polymer being in a second conformation and having sufficient rigidity whereby the structure is held in the second conformation, wherein upon hydration of the hydrophilic polymer the structure assumes the first conformation. In a preferred embodiment, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

In accordance with a sixth aspect of the present invention, there is provided a medical device designed for internal use in a patient, comprising a structure, the structure comprising a first material preconfigured into a first conformation and a hydrophilic polymer material preconfigured into a second conformation, the first material and the hydrophilic polymer having respective mechanical strengths, the mechanical strength of the hydrophilic polymer material exceeding that of the first material sufficiently so that the structure is in the second conformation, wherein the hydrophilic polymer material is adapted to lose its mechanical strength upon the occurrence of a triggering event and upon loss of the mechanical strength of the hydrophilic polymer, the device assumes the first conformation.

In a preferred embodiment, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches,

modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the triggering event is an increase in temperature. Or, alternatively, the triggering event is hydration of the hydrophilic polymer material. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

In accordance with a seventh aspect of the present invention, there is provided a method to manufacture a medical device having shape memory properties, comprising: providing a medical device comprising a first material formed into a first conformation; applying a hydrophilic polymer to at least a portion of a surface of the device; deforming the device from the first conformation into a second conformation under conditions designed to permit the device to retain a memory of the first conformation; and allowing the hydrophilic polymer to harden and hold the device in the second conformation.

Preferably, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In a preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

In accordance with an eighth aspect of the present invention, there is provided a method to manufacture a medical device having shape memory properties, comprising: providing a medical device comprising a first material and a first polymer formed into a first conformation, the first material and the first polymer having respective mechanical strengths, the first polymer being capable of losing its mechanical strength upon the occurrence of a triggering event; and deforming the device from the first conformation into a second

conformation under conditions designed to permit the device to retain the memory of the first conformation and to permit the mechanical strength of the first polymer to hold the device in the second conformation.

In a preferred embodiment, the second polymer is a hydrophilic polymer. In such embodiment, preferably, the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof. In another preferred embodiment, the triggering event is an increase in temperature. In still another preferred embodiment, the triggering event is hydration of the second polymer material. In another preferred embodiment, the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be better understood by reference to the figures of the drawings wherein like numbers denote like parts throughout and wherein:

Figures 1A-1C illustrate, in sectional view, a stent in accordance with an embodiment of the invention after insertion in the ureter but before expansion (1A), after expansion (1B) and the stent both before (a) and after (b) expansion (1C);

Figures 2A-2D illustrate, in sectional view, a stent in accordance with another embodiment of the invention after insertion in the ureter but before expansion (2A), after expansion (2B), the stent both before (a) and after (b) expansion (2C) and the insertion of the stent (2D);

Figures 3A-3C illustrate, in views similar to Figures 1A-1C, a stent in accordance with yet another embodiment of the invention;

Figure 4 illustrates, in partial view, in section, an anchoring structure useful with various embodiments of the invention;

Figure 5 illustrates, in partial side view, another anchoring structure useful with various embodiments of the invention;

Figures 6A and 6B illustrate, in partial view in two different positions of operation, an insertion structure useful with various embodiments of the invention;

Figure 7 illustrates, in partial view, a variation of the insertion structure of Figure 6;

Figure 8 illustrates, in partial view, another insertion structure useful with various embodiments of the invention;

Figure 9 illustrates, in partial view, yet another insertion structure useful with some embodiments of the invention; and

Figure 10 illustrates, in partial view, a stent with internal ribs.

Figure 11 schematically illustrates a method for introducing shape memory into a medical device, such as a stent.

Figure 12 illustrates a stent manufactured with shape memory with Figure 12a showing formation of the stent in a first conformation, Figure 12b showing reconfiguring of the stent into a second conformation with a surface coating of a hydrogel, and Figure 12c showing reversion of the stent to the first conformation upon hydration.

BEST MODE FOR CARRYING OUT THE INVENTION

In accordance with the present invention, there is provided a medical device that is adapted for easy insertion or implantation into a patient but that will change size or shape to assume a configuration different than the configuration prior to insertion or implantation. In general, such ability of the device to change conformation or configuration is made possible by manufacturing a device having a first conformation or configuration and, thereafter, reversibly reconfiguring the device into a second conformation or

configuration. In connection with reversibly reconfiguring the device into a second conformation or configuration, the term "reversibly" ordinarily includes making the device capable of assuming the first conformation or configuration upon the occurrence of a triggering event. Events such as temperature changes and hydration or combinations thereof are contemplated. As will be appreciated, what, in essence, is achieved in the present invention is a unique method to control, or provide, "shape memory".

Through the use of shape memory, in general, it is possible to configure a device into a particular, advantageous, configuration. Then, after insertion or implantation into a patient, the device is capable of reverting into a predetermined shape. For example, in the case of stents, it is often desirable to have stents possess end pigtails or enlarged end diameters so that they are not ejected from the duct or do not slide from their place of insertion.

Inclusion of such pigtails or enlarged ends, however, makes insertion of the stents more difficult. While the stent can be mechanically held in a more convenient shape (i.e., straightened out over a guidewire, clamped, or tied), this adds either steps or levels of difficulty to the insertion procedure. Moreover, it is necessary for the physician to take a positive step to release or otherwise remove the mechanical holding.

Accordingly, provision of shape memory in a medical device is preferable. In accordance with the invention, the change from an easy insertion or implantation configuration to the second retention configuration is automatic; it is triggered by the body. In accordance with the invention the trigger can be accomplished by either temperature or hydration (i.e., bodily fluid activation) or a combination thereof. In preferred embodiments, the trigger is accomplished by bodily fluid contact. Moreover, where the trigger is accomplished by contact with a bodily fluid, the effect can be accentuated by temperature change.

Identical concerns that are mentioned above with respect to stents are also applicable in the catheter and intubation arts, which include, without limitation: intravenous catheters, guiding catheters, sheaths, umbilical catheters, trocar

catheters, heart catheters including, valvostomy catheters, angioplasty catheters, arthroscopy catheters, and the like), perfusion catheters, suction catheters, oxygen catheters, endoscopy catheters, endotracheal tubes, stomach tubes, feeding tubes, lavage tubes, rectal tubes, urological tubes, irrigation tubes, aneurysm shunts, stenosis dialators, trocars, and inserters, generally. Occasionally it is desirable to insert such tubes or catheters in a first configuration or conformation and, after insertion, have them change to a second configuration or conformation. For example, as shown in Fuqua, U.S. Patent No. 4,710,181, the disclosure of which is incorporated by reference herein, a folded catheter is held within a sheath to maintain a low profile during insertion. Following insertion, the sheath can be removed, which will allow the folded catheter to expand to its full diameter. A similar result can be accomplished through the shape memory techniques of the invention. For example, through the shape memory techniques of the invention, the device can be manufactured to increase in diameter upon insertion. Alternatively, a sheath system can be used where a device is inserted within the sheath and the sheath is designed to lose its mechanical strength and release the interned device.

Similarly, in the case of intraocular lenses, it is often desirable to have the lenses folded for insertion. This has typically been accomplished by clamping the lenses in half. Through use of shape memory technology, lenses can be manufactured in a first open configuration, reconfigured into a second folded configuration, sold in such folded configuration, and, upon insertion into an eye of a patient, will open to the first configuration.

Accordingly, it will be appreciated that the provision of shape memory has broad applicability in the medical device art. In particular, devices that are designed for implantation or insertion in the body are improved in accordance with the invention. Thus, shape memory is an attractive method for overcoming the inconveniences and problems associated with changing a configuration or conformation of a medical device *in vivo*.

There are several approaches that can be used to achieve shape memory

in accordance with the invention. Preferably, for example, reconfiguring the device is accomplished by, in appropriate cases, heating the device and manipulating the device to a second conformation or configuration. Alternatively, reconfiguring in another preferred embodiment is accomplished by manipulating the device to a second configuration or conformation and applying a substance that will cause the second conformation or configuration to be maintained. For example, a hydrogel may be applied to selected portions of a polymeric medical device which will reversibly hold the device in the second conformation or configuration until the device is exposed to water at which time it will revert to the first conformation or configuration.

In a closely analogous embodiment, a device may be manufactured from a composite polymeric matrix including generally hydrophobic and hydrophilic polymers. For example, an interpenetrating matrix of a hydrophilic and a hydrophobic polymer as described in U.S. Patent Nos. 4,883,699 and 4,911,691, the disclosures of which are hereby incorporated by reference. If appropriately manufactured (i.e., including appropriate ratios of the hydrophobic and hydrophilic polymer mixtures) the device can be manipulated, while hydrated, into a second conformation and allowed to dry while being maintained in a second conformation or configuration. Thereafter, when the device is rehydrated, it will return to the first configuration or conformation. Devices manufactured from an interpenetrating network, for example, can also be fashioned through the use of heating as mentioned above.

These separate embodiments can be viewed in several basic categories of reconfiguring of the device from the first conformation to the second conformation: thermal processing, surface coating, interpenetrating network technologies, and combinations thereof. Each of these technologies will be discussed serially below.

I. Thermal Processing

Referring now to Figures 11a through 11e, a stent 700 is provided having

a distal end 701. The stent 700 is formed from a composite of polymers having disparate glass transition temperatures. Preferably, one of the polymers has a glass transition temperature at about body temperature referred to herein as the "first polymer" and another of the polymers has a glass transition temperature at a temperature significantly exceeding the glass transition temperature of the first polymer, referred to herein as the "second polymer."

In Figure 11a, while the stent 700 can be manufactured in any shape, it is pictured in the Figure in a straight configuration. In manufacture, for example, the stent 700 can be melt extruded in a straight configuration or molded into another configuration. The stent 700, or other medical device, can be manufactured as an interpenetrating network of polymers (as described in U.S. Patent No. 4,488,699, the disclosure of which is hereby incorporated by reference).

Alternatively, the medical device can be manufactured in discreet polymer layers (as described in U.S. Patent Nos. 4,627,844, 4,636,346, 4,846,812, and 4,994,047, the disclosures of which are hereby incorporated by reference).

Referring now to Figure 11b, the stent 700 is heated to a temperature above the glass transition temperature of the second polymer and shaped into an appropriate shape. In the illustrated embodiment, a partial pigtail 702 is formed in the distal end 701 of the stent 700. Shaping can be accomplished using appropriate mandrels and/or shaping tools which are well known to those of skill in the art. This configuration is referred to as the first configuration. Generally, the stent is cooled to a temperature below the glass transition temperature of the first polymer after being configured in the first configuration while it is maintained in the first configuration. As will be appreciated, the stent may be cooled to a temperature below the first or second polymer. The primary purposes of the cooling step are to enable the ease of handling of the device and also to provide memory to the device of the first conformation.

Thereafter, in Figure 11c, the stent 700 can be heated to a temperature exceeding the glass transition temperature of the first polymer and shaped into

a second configuration. Necessarily, the polymers are selected so that the glass transition temperature of the first polymer is lower than the forming temperature of the second polymer. In this way, the "memory" of the first configuration is retained by the polymer. Then, the stent 700, or other medical device, formed into the second configuration, is cooled below the first polymer glass transition temperature while it is maintained in such configuration.

As illustrated in Figure 11d, the stent 700 formed into the second configuration is then easily inserted into the body, herein pictured during insertion into through the ureter 750 and into the kidney 751 of a patient. Insertion is accomplished in any conventional manner, such as insertion through the urethra (not shown) and traversing through the bladder (not shown) using a guidewire or other insertion device. As shown in Figure 11e, Upon insertion as described, the stent 701 will heat to a temperature approaching or exceeding the glass transition temperature of the first polymer. At such temperature, the mechanical strength of the first polymer will become insufficient to hold the second configuration and the stent 700 will revert to the first configuration. Such shape is the shape dictated by the shape which it was given in Figure 11b (i.e., the first configuration). As will be appreciated, the shape in Figure 11b was dictated by the glass transition temperature of the second polymer which allowed configuring of the device into the first configuration.

Methods to manufacture medical devices from composite polymers with appropriate glass transition temperature characteristics are well known to those of ordinary skill in the art. As well, appropriate polymers to meet the shape memory objectives of the invention will be readily selectable by those of skill in the art without undue experimentation.

A limitation of medical devices manufactured through the thermal processing techniques described above, is that during shipping, storage, insertion, implantation, and the like, it is expected that the glass transition temperature of the second polymer may be prematurely attained and the device will revert from the second configuration to the first configuration before it is desirable. While,

in many situations, it may be possible to clamp or otherwise package devices so that the problem is minimized, it would be preferable to avoid the problem more completely.

Accordingly, the following embodiments are provided where effects of elevated temperatures will be less deleterious to maintenance of the second conformation or configuration.

II. Surface Coating

In accordance with another embodiment of the invention, bodily fluid softenible polymers or other coatings can be used to hold a device in a second configuration or conformation after manufacture in a first configuration. This technique closely follows the illustrations provided in Figures 11a through 11e with reference to a stent 700.

As described in connection with Figure 11 (relating to thermal processing), the medical device is first configured into a desired first configuration or conformation. In a preferred embodiment, this is accomplished in Figures 11a and 11b, where the stent 700 is formed into a desired shape. As will be appreciated, the stent can be formed in one configuration (i.e., straight (Figure 11a)) and thereafter shaped into the first configuration (Figure 11b). Or, the desired first configuration can be formed in a single step.

In Figure 11c, the stent 700 is formed into the second configuration. To accomplish this change in conformation or configuration, the stent 700 in Figure 11b is surface coated with a material, referred to herein as the softenible material, that has sufficient mechanical strength to hold the device in a second configuration that will soften, erode, or dissolve away (generally, lose its mechanical strength) upon exposure to a bodily fluid (i.e., hydrated), upon attaining a temperature near body temperature, or a combination. Following surface coating of the stent 700 with the softenible material, the stent 700 is manipulated into the second conformation and the coating is allowed to harden which will hold the stent 700 in the second configuration.

In a preferred embodiment, the softenible material is a polymer that is generally hydrophilic, such as poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly(hydroxy ethyl acrylate), poly (hydroxy alkyl methacrylate) (such as poly(hydroxy ethyl methacrylate) (poly(HEMA))), hydrophilic polyurethanes, HYPAN and oriented HYPAN (block copolymers of polyvinylalcohol and polyacrylonitrile, made by selectively hydrolyzing blocks of the polyacrylonitrile), HEPU (hydrophilic polyurethane block copolymers with polyethylene oxide), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, a starch such as cornstarch, a modified starch, an alginate, a hydroxy ethyl carbohydrate, or the like. In highly preferred embodiments, the softenible material is a hydrogel, such as polyethyleneoxide available from Union Carbide, or polyvinylpyrrolidone, available from BASF.

Thereafter, as shown in Figures 11d and 11e, when the stent 700 is inserted into the body, the softenible surface coating will lose its mechanical strength and the stent 700 will return to the first configuration.

In this embodiment, the medical device is typically formed of a polymer material. Generally, any biocompatible polymer will be acceptable. When implantation or relatively long indwelling time periods are required of the medical device, generally highly biocompatible polymers are used.

Surface coating can be accomplished through a variety of processes that are well known to those of ordinary skill in the art. For example, surface coating may be accomplished by dipping, spraying coextruding, laminating, and/or injection molding the coating onto a substrate polymer. Moreover, surface coating can be accomplished on either an "internal" or an "external" surface of the device. For example, in the case of a stent or a catheter, a surface coating may be applied to the external surface of the article or it may be applied inside of the lumen with equal success. One advantage of external surface coating is ease of application. However, the ease of application will, in certain situations, be outweighed by an advantage of internal coating which includes the

ability to maintain a lower profile of the device. When the surface coating is internal to the device, the coating will soften, expand, dissolve away, or otherwise loose mechanical strength and allow the device to revert to the first conformation or configuration. Where the surface coating does not dissolve away or otherwise open the lumen, the lumen will need to be made of a large enough diameter to be efficacious for the intended purpose.

Nevertheless, a limitation of simple surface coating comes when the softenible surface coating simply dissolves away from the device. If the softenible coating is designed to dissolve away, the material forming the coating will be introduced into the patient's body. Therefore, the material must be highly biocompatible in order to avoid causing deleterious effects in a patient's body. Examples of preferred materials include polyvinlypyrrolidone, polyethylene oxide, poly(HEMA), polyvinylalcohol, starches, alginates and cellulose. Alternatively, the surface coated device can be cross-linked to limit or prevent solvation of the coating. As will be appreciated, through appropriate amounts cross-linking, the coating will be less soluble in bodily fluids but will still undergo softening, expansion, or loss of mechanical strength to achieve the intended result. The amount of cross-linking necessary for a given application can be readily determined by those of ordinary skill in the art by routine experimentation.

III. Interpenetrating Network Technology

In a closely analogous manner to that discussed for surface coating, above, an interpenetrating network of a hydrophobic and a hydrophilic polymer can be formed. However, in this embodiment, there is no step of surface coating. Rather, the device is manufactured as a composite of materials: one that is relatively hydrophilic and another that is relatively hydrophobic or non-hydrophilic. There are several methods that can be used for the manufacture of medical devices formed with interpenetrating networks that will have shape memory.

For example, in manufacture, the device may be hydrated (i.e., exposed to a fluid resembling a bodily fluid or water) and shaped into a second conformation or configuration. Thereafter, the device is allowed to harden in a second conformation. Then, upon insertion or implantation into the patient, the device will become hydrated and return to the first configuration.

Alternatively, the device can be manufactured using the techniques described above for thermal processing. However, rather than using temperature (primarily) as the trigger for causing a change in conformation from the second configuration to the first configuration, swelling or loss of mechanical strength of the hydrophilic polymer in the interpenetrating network is utilized.

The process of manufacture, in either case, closely follows the procedure discussed in connection with Figure 11.

Medical devices formed from interpenetrating networks that are given shape memory properties are highly desirable since none of the polymers are washed away and diffused throughout the body of a patient. Instead, the hydrophilic polymer is a part of the polymer matrix of the device and is retained as part of the structure of the device. The hydrophilic polymer, which in its non-hydrated state, acts to hold the device in the second conformation, simply loses its mechanical strength and allows the shape dictated by the hydrophobic or non-hydrophilic polymer to be assumed, i.e., the first conformation.

IV. Discussion of Material Technology

As was mentioned above, the invention has broad applicability to the medical device field. Certain preferred embodiments are described below, particularly relating to the stent art and more particularly relating to uretal stents. However, as will be appreciated to those of ordinary skill in the art, such embodiments are illustrative rather than limiting.

The hydrophilic component is suitably a polymer that absorbs at least about thirty percent (30%) water, preferably at least about fifty percent (50%) water, more preferably about one hundred percent (100%) water or more, e.g., one hundred fifty percent (150%) water, by weight based on the weight of the hydrophilic polymer. The hydrophilic polymer, preferably, is capable of forming a hydrogel upon absorption of water.

The hydrophilic polymer can suitably be selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly(hydroxy ethyl acrylate), poly(hydroxy ethyl methacrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, a starch such as cornstarch, a modified starch, an alginate, a hydroxy ethyl carbohydrate, or the like. Copolymers of the monomers forming such polymers are also suitable. Mixtures of any of the above are likewise suitable. The polymer should preferably allow the device to swell to a selected percent after hydration.

The degree of swelling of the hydrophilic component, and consequently, the device, can also be controlled or tailored as desired by controlling the amount of cross-linking of the polymer. The amount of cross-linking can be adjusted, as is well known in the art, chemically and/or by adjusting the amount of radiation applied to cause the cross-linking. The higher the degree of cross-linking, the less will be the swellability of the hydrated polymer and thus of the particular device.

The device preferably comprises a hydrophilic component and a non-hydrophilic component in a selected ratio. The ratio of hydrophilic component

to non-hydrophilic component is preferably adjustable so as to allow the polymer to expand the initial cross ureteral stent outer diameter d to a desired extent, for example, by from about five percent (5%) up to about three hundred percent (300%), or more preferably from about fifteen percent (15%) up to about fifty percent (50%), upon hydration.

The polymer can be formulated so that upon hydration one portion of a device, the device softens to a greater degree than does another portion of the device. To achieve this dual hardness after hydration, initially the device can be processed differently at different positions of the device. For example, one portion of the device can be cross-linked more than is another portion of the device, e.g., by exposing it to more polymerization initiating radiation. This can be accomplished through shielding or other conventional methods, such as bonding dissimilar components which is often referred to as butt joining.

While devices in accordance with the invention can be formulated of a polymer which comprises only a hydrophilic component, preferably the device will also comprise a non-hydrophilic component. The non-hydrophilic component comprises a polymer which does not substantially absorb or attract water. Preferably, the non-hydrophilic polymeric component is capable of absorbing water in an amount of no more than about thirty percent (30%), more preferably no more than about fifteen percent (15%) and still more preferably no more than about ten percent (10%), by weight, based on the weight of the non-hydrophilic polymeric component.

The non-hydrophilic component can be, for example, a thermosetting elastomer such as silicone, a polyurethane such as an aliphatic or aromatic polyurethane, a polyether polyurethane, a polyester polyurethane, and a polycarbonate polyurethane; an ethylene copolymer such as ethylene-vinyl acetate copolymer; a polyamide, in particular a polyamide of low crystallinity; an aliphatic polyester or mixtures or copolymers thereof. In addition, the nonhydrophilic component may include a metal and, in particular, certain shape memory metals, such as Nitinol, tungsten, tantalum, and other similar metals.

The nonhydrophilic component, as will be appreciated can be provided in solid or other form, such as in a mesh.

Examples of swelling (and softening) polymers having both hydrophilic and non-hydrophilic components and which are useful in the practice of the invention are those described in, for example, U.S. Patent 4,883,699, issued November 28, 1989 which is incorporated herein by reference.

This patent discloses a suitable composition for the polymer which comprises: (a) a first phase which comprises a substantially non-hydrophilic polymeric component; and

(b) a second phase which comprises a hydrophilic polymeric component;

said material (i) being capable of absorbing water to an extent that it swells with a swelling ratio of at least about 1.3:1, preferably from about 1.5:1 to 3.5:1 (and generally softens with a softening ratio of at least about 2:1).

Also useful are those swelling and softening hydrophilic polymers described in U.S. Patents 4,359,558; 4,424,305; 4,454,309 and 4,439,583 of Tynsdale Plains-Hunter Ltd. incorporated herein by reference. The preferred polymer composition of these patents essentially comprises a polyurethane diacrylate composition having from about ninety (90) to about sixty five (65) weight percent of a hydrophilic polyurethane resin and from about ten (10) to about thirty five (35) weight percent of a diacrylate.

Still another polymer which is suitable is the thermoplastic elastomeric hydrophilic polyurethane described in U.S. Patent 5,061,254 of Becton-Dickenson and Company which is incorporated herein by reference.

In accordance with one embodiment of the invention, the device can be formulated of a physiologically acceptable polymer that is capable of softening and expanding to a predetermined degree upon hydration then subsequently shrinking to a desired extent, for example, to roughly its non-hydrated size, to allow it to be readily withdrawn from the patient after a desired length of time. To accomplish this, the polymer can comprise a soluble hydrophilic component and a non-soluble non-hydrophilic component having softening and expansion

characteristics as previously described. The hydrophilic component and non-hydrophilic component can be selected from the respective groups indicated above. As the hydrophilic component dissolves or degrades the device will then shrink.

As another alternative, the device can be formulated of a central cylindrical core of a physiologically acceptable polymer that is capable of softening and expanding to a predetermined degree upon hydration but that will not dissolve or biodegrade readily in the ureter or in another selected duct or bodily cavity. The device can further include an outer layer formulated of a physiologically acceptable polymer that is readily soluble or biodegradable in the ureter. For example, the outer layer can be a substantially non-cross-linked hydrophilic polymer. The dissolving of all or part of the outer layer then leads to a subsequent-to-insertion shrinking of the device to a desired extent, for example, to roughly its non-hydrated size, to allow it to be readily withdrawn from the patient after a desired length of time.

The expansion and softening of a non-hydrated device normally occurs from within forty five (45) minutes to a few hours after its insertion into the body of a patient. The subsequent shrinking of the device to its non-hydrated size or smaller usually takes from three days to three months as the soluble (or degradable -the term soluble is used herein to encompass all means by which the device shrinks) component is dissolved or degraded from the device. The rate of shrinking and the final shrink size can be controlled by the volume ratio of hydrophilic component to non-hydrophilic component and/or the extent to which the hydrophilic component is cross-linked. The higher the initial volume of soluble component, the smaller the size of the device after the soluble component has dissolved. In addition, the higher the degree to which the soluble component is cross-linked, the slower the rate at which the soluble component will dissolve and thus the slower the rate at which the device will shrink.

The shape and/or expansion of a device can also be controlled by beginning with a non-hydrated device with substantially a constant outer diameter

along its length, heating the non-hydrated device above the forming temperature of the non-hydrophilic component, which is above the melting temperature of the hydrophilic component, while in contact with a first mandril which molds the device to a different configuration, followed by cooling the device below the melting temperature of the hydrophilic component while it is still shaped by the first mandril, removing the device from the first mandril, positioning the device on a second mandril which defines a substantially different shape or configuration, heating the device to a temperature above the melting temperature of the hydrophilic component but below the forming temperature of the non-hydrophilic component, molding the device against the second mandril, and cooling the device to a temperature below the melting temperature of the hydrophilic component while it is still shaped by the second mandril. On later insertion into the body, hydration of the hydrophilic component, which substantially reduces the strength of the shape set by the hydrophilic component, allows the shape molded against the second mandril to be lost and the device will return to the shape molded against the first mandril.

In each of these embodiments, shape memory is introduced into the stent or other device through use of interpenetrating network technology utilizing a thermal-type processing. It will be appreciated that these embodiments could also be manufactured using a surface coating (described above) that would act to hold the stent in its preinsertion conformation and then would dissolve away or soften to allow expansion or formation of the desired shape. Alternatively, the hydrophilic polymer can be hydrated and the device configured into the first conformation and dried in the second configuration. Upon hydration, the device will assume the first conformation, i.e., an enlarged diameter.

Useful biodegradable polymers include polyorthoesters, polylactides, polyglycolides and copolymers, collagen, polycaprolactone and polyglutonates. One suitable biodegradable polymer comprises L(-)lactide, glycolide and epsilon-caprolactone in selected ratios. An example of a biodegradable polymer having L(-)lactide, glycolide and epsilon-caprolactone which is useful in the practice of

the invention is described in U.S. Patent No. 5,085,629 issued February 4, 1992 which is incorporated herein by reference.

Suitable dissolvable polymers include polyethylene oxides, polyvinylacetates, polyvinylpyrrolidone, polyethylene oxide based polyether urethanes, starches and cellulose derivatives such as hydroxyethyl cellulose. The dissolvable polymers are generally preferred since they can be readily formulated so as to dissolve in minutes to hours. The rate at which the polymer hydrates and degrades can be controlled by controlling the molecular weight and the amorphous nature of polymer composition.

Mineralization with agents such as cholesterols, uric acids and cystines, and calcification, particularly with agents such as calcium phosphate, calcium oxalate, struvite, brushite, and calcium apatite, can be inhibited by various chemicals. Such inhibitory chemicals can be incorporated into implants, stents, and devices by the various methods referenced above. Anti-calcification chemicals or additives are known in the art and include certain diphosphonates, especially ethanehydroxy diphosphonate (EHDP), certain metal ions, especially aluminum and iron and alpha amino oleic acid derivatives to name but a few. For example, hydroxyethylidene biphosphonic acid dispersed in polyurethane (PU) articles inhibits calcification of the polymer and of the surrounding tissue and EHDP can diffuse through PU membranes and inhibit calcification of tissue. Aluminum or iron ions and oleic acid compounds have all been reported to reduce calcification of bioprosthetic porcine heart valves. Anticalcification techniques are disclosed in U.S. Patent No. 4,753,652, the disclosure of which is hereby incorporated by reference.

It will also be appreciated that a variety of other diagnostic and therapeutic agents can be incorporated into polymers in a manner adapted to allow the agent to be released and allow diagnosis and/or therapy. For example, in the intravenous art there is a great deal of current interest in the prevention of restenosis. Agents designed to prevent restenosis may be capable of delivery through incorporation within the polymers of the present invention. For a review

of certain of the current strategies for preventing restenosis, *see* Epstein et al. *J Am Coll Cardiol* 23(6):1278-88 (1994) the disclosure of which is hereby incorporated by reference. In antitumor applications, there are a huge number of potential chemo- and radiotherapeutic agents available. *See* Calabresi et al. *Antineoplastic Agents* pp. 1209-63 in "The Pharmacological Basis of Pharmacology" (Goodman et al. 8th ed. Permagon Press (1990)), the disclosure of which is hereby incorporated by reference. Such agents can be incorporated into polymers and can be delivered to a tumor site, such as in ductal tumors. Similarly, antimicrobial agents can be suitably incorporated into and released from polymer structures. Some exemplary antimicrobial agents are described in Sande et al. *Antimicrobial Agents* pp. 1018-1201 and Webster et al. *Chemotherapy of Parasitic Infections* pp. 954-1017, both in "The Pharmacological Basis of Pharmacology", *supra.*. Hormones, in particular growth hormones, can also be delivered through use of the present invention. Examples of appropriate hormones are described in Murad et al. *Hormones and Hormone Antagonists* pp. 1332-1522 in "The Pharmacological Basis of Pharmacology", *supra.*

In order to achieve the purposes of the present invention a variety of techniques can be used. In general, as described above, the present invention in one aspect may be summarized as the use of a first material to hold a second material in a defined shape so the material may be inserted or implanted into the body and then upon a triggering event change shape. In a preferred embodiment, a hydrophilic material is used as the first material for the purpose of holding the second material in the defined shape. The triggering event, in such embodiment is an act of hydration of the hydrophilic material which results in a general softening and/or loss of mechanical strength of the hydrophilic polymer. Such softening and/or loss of mechanical strength releases the second material from the defined shape in which it was held by the first material.

EXAMPLES

Example 1. <u>Preparation of a Shape Memory Stent Using Surface Coating</u>

In this example, a surface coating of a hydrophilic polymer is used as a first material to hold a second interpenetrating network material in a predetermined position. In this example, the hydrophilic polymer loses mechanical strength upon exposure to a bodily fluid so that the second material is capable of returning to a shape that it was conformed into prior to coating with the first material.

Referring to Figures 12a through 12c, a shape memory uretal stent was prepared using a stent 800 formed from an Aquavene™ interpenetrating network using polyurethane as the non-hydrophilic polymer and polyethyleneoxide, polyvinylpyrrolidone, or polyvinylalcohol as the hydrophilic polymer as described in U.S. Patent No. 4,994,047. The stent 800 was melt extruded in a straight configuration. The stent 800 had a connecting section 801 and end sections 802 and 803. Pigtails 804 and 805 (540^0) were formed on each of the end sections 802 and 803 of the stent 800 (FIG. 12a) through heating the stent to 105°C for 60 minutes and holding in a conventional mandrel to form the first configuration (FIG. 12a).

The pigtails 804 and 805 on the stent are partially straightened or uncoiled to 270^0 and surface coated with a hydrogel polyvinylpyrrolidone, polyvinylalcohol, or polyethyleneoxide which was allowed to harden and hold the stent 800 in a second configuration (FIG. 12b) to form connecting section extensions 806 and 807. Upon hydration (FIG. 12c), the connecting section 801 and the end sections 802 and 803 of the stent 800 expanded in length and diameter due to the hydration of the hydrophilic polymer in the interpenetrating network. Moreover, the hydrogel on the connecting section extensions 806 and 807 dissolved away, recoiling the pigtails to their first configuration of 540^0.

As will be appreciated, the first configuration allowed easy insertion of the stent 800 into a ureter in a patient since the 270^0 coils could be easily straightened over a guidewire yet assist in retaining the stents position on insertion. Further, the expansion (of both diameter and length of the connecting

section 801) allowed for good flow through the ureter and kept the stent 800 at a constant length even with the recoiling of the pigtails 804 and 805.

Example 2. <u>Preparation of a Shape Memory Stent Utilizing an Interpenetrating Network Polymer System and Thermal Shaping</u>

In this example, a catheter is formed from an interpenetrating network polymer system including a hydrophilic and a non-hydrophilic polymer. In the interpenetrating network system, the hydrophilic polymer is utilized as the first polymer which acts to holds the second (non-hydrophilic polymer) in a desired conformation. Such desired conformation until such time as the catheter is contacted with a bodily fluid and the hydrophilic polymer within the interpenetrating network loses its mechanical strength. At that time, the catheter will revert to a shape dictated or allowed by the second non-hydrophilic polymer.

The catheter is formed as described in Example 1. The catheter is shaped into a urinary stent with a small radius (i.e., ¼ inch), multiple pigtail (i.e., 360° or greater) on each end as discussed in Example 1. The pigtails are formed using a forming temperature above the melting point of the hydrophilic component and below the melting point of the non-hydrophilic component. This forming temperature sets a pigtail shape in both components (referred to as the first configuration).

The urinary stent may then be reshaped to a larger radius (i.e., ½ inch), partial pigtail (i.e., less than or equal to 270°) and in some cases may be completely straightened on a new forming tool. As repositioned in this new shape, the stent has assumed the configuration. Generally, it is set in this shape using a temperature below the forming temperature of the non-hydrophilic component, but above the forming temperature of the hydrophilic component. The stent is then cooled in the second configuration for insertion into the body. The hydrophilic component holds the non-hydrophilic component in the second configuration.

During hydration (inside the body) the hydrophilic component loses its

mechanical strength and becomes soft and flexible, thus allowing the non-hydrophilic component to resume its original shape (the first configuration) which has more coiling and a smaller radius and possibly a greater retention force and any geometry may be achieved.

Example 3. Preparation of a Shape Memory Stent Utilizing an Interpenetrating Network Polymer System and Hydration

In Example 2, the stent was reformed from the first to the second configuration through heating the catheter to a temperature that would soften the hydrophilic component but does not soften the non-hydrophilic polymer. Typically, the temperature exceeds the forming temperature of the hydrophilic component. As an alternative to the use of heat to reform a polymeric device in accordance with the invention, it is also possible to use hydration followed by drying or hardening to lock the device into the second conformation.

In this embodiment, the same product configurations as in the above examples are used. However, rather than heating the stent to a temperature above the forming temperature of the hydrophilic component but below the forming temperature of the nonhydrophilic component and changing the configuration, the stent (in the first configuration) may be reshaped into the second configuration through hydrating the device and holding the hydrated device in a second configuration while it dries.

This embodiment is useful in situations where the melting of the hydrophilic component is not acceptable. For example, in certain situations, an excessively high melt temperature of the hydrophilic component could have undesirable effects on the non-hydrophilic component. In addition, excessive temperatures could cause an additive, in the hydrophilic component (such as a medicament or drug) to be degraded. Further, it is also possible to include medicaments or drugs in the aqueous solution that is used for hydration. Such drugs or medicaments can be taken up by the hydrophilic component, retained while it is dry or hardened, and released upon insertion or implantation into a

patient.

Example 4. Preparation of a Shape Memory Intraocular Lens

In another embodiment, an intraocular lens (IOL) is fabricated from a shape memory polymer, including an interpenetrating network, in accordance with the present invention. In such embodiment, the IOL can be formed into a folded position (as the second configuration) from its open conformation (as the first configuration) prior to insertion into a patient. The second configuration allows a smaller incision to be made into the patient's eye, and, reduces trauma.

The triggering event for the conversion from the second configuration of the IOL to the first configuration of the IOL may be selected from any of a variety of events. For example, a temperature sensitive polymer may be used to form the lens. In such embodiment, when the IOL is inserted and upon reaching body temperature the IOL would reform from the folded (second configuration) to into the unfolded (first configuration) shape. Thus, the IOL will be in a configuration for remaining in position in the patient's eye and correcting his or her vision in a manner similar to that described in Stoy U.S. Patent No. 4,731,079.

Example 5. Preparation of a Shape Memory Intraocular Lens

In the Stoy patent, a disadvantage to heat trigger approach is evident. It is likely that temperatures, higher than body temperatures, will be experienced by the IOL during the shipping and/or storage of this device. Therefore, the patent taught that it was necessary to store the device in a clamped position within its packaging and to cool the device prior to insertion. Alternatively, the IOL could be fabricated on-site so that temperatures could be controlled. Either of these approaches add a great deal of complexity to the procedure.

These limitations are also applicable in connection with the IOL disclosed in connection with Example 4. Therefore, in this example, another shape memory approach that is relatively insensitive to temperature is provided. Such

approach eliminates much of the complexity described above. In the procedure, the IOL is coated, either through a surface coating or through use of an interpenetrating network, with a hydrophilic polymer that is stiff/rigid when dry or hardened, and will not soften at temperatures experienced during shipping and storage.

For surface coating applications, one appropriate hydrophilic polymer is polyvinyl pyrrolidone (PVP) which is biocompatible and has been used in the eye, and would not melt at temperatures below 90°C (195°F). After IOL is processed appropriately, and pre-folded, the IOL could be dipped into a liquid solution of PVP and dried. Once placed within the body, the body fluids would dissolve the PVP, and allow the IOL to resume the shape upon reaching body temperature.

Example 6. Preparation of a Shape Memory Catheter

In this embodiment, virtually any catheter which includes an internal lumen may be provided with shape memory properties through the coating of the internal lumen with a dissolvable layer, such as a hydrogel. Several advantages are conferred by surface coating with a dissolvable material within the internal lumen. For example, a very low profile catheter can be used, since the coating will be internal. As the coating is dissolvable, the coating will dissolve and will be free to flow from (or otherwise be removed from the lumen) upon hydration/dissolution of the coating and the lumen will be open. A non-dissolvable coating can also be used (such as an interpenetrating network), however, the lumen will not open as it would with a dissolvable coating.

A catheter with the hydratable material in the internal lumen will behave in a similar manner as the devices discussed in Examples 1-3.

It is also possible to use the internal dissolvable coating approach for the preparation of low profile catheters with initial high pushability, followed by extreme flexibility. This is accomplished in accordance with the invention through the fact that a hydrogel (or other dissolvable polymer) can be utilized to

hold the catheter in a initial fixed or rigid conformation (such as straight). Such rigid conformation will be easily advanced through a duct or vasculature in a patient. As the dissolvable layer is contacted with bodily fluids the catheter will lose some of its rigidtiy and will increase in flexibility. These aspects are advantageous for urethral, uretal, and cardiovascular applications.

As was mentioned above, while certain of these shape memory features can be obtained through the use of heat triggers (features such as longitudinal stretching and folded-in reduced diameter catheters (i.e., Fuqua U.S. Patent No. 4,710,818)), heat sensitive polymers pose the problem of premature release. Therefore, by coating the inner lumen with a hydrogel, the device is held in its proper shape until fluid flow through the lumen begins and softens the hydrogel thereby allowing the device to change shape or rigidity.

In the case of urethral and uretal catheters, it is desirable to have sufficient working time to place the catheter far enough through the urethra to allow flow from the bladder to begin before the shape changes. This is very important and beneficial in the case of pediatric urethral catheters which are usually so small that the flow through the tube is especially slow, but cannot be made faster by a larger tube due to size constraints of the child's urethra. Additionally, a stiffer/smaller tube can be inserted which will soften considerably for patient comfort once the hydrogel has softened.

Example 7. Preparation of Shape Memory Catheter

Another example of a shape memory catheter in which a first material holds a second material until the first material is hydrated inside the body again uses the principle of coating catheters to hold them in different configurations.

In this example, a conventional urinary stent prepared from silicone, polyurethane, or another suitable material may be shaped with pigtails at each end as described in Example 1. This catheter configuration including the pigtails is in the first configuration. The catheter may then be straightened partially or completely on a rod and coated with a hydrophilic polymer. The hydrophilic

polymer after drying, curing, or hardening will hold the urinary stent straight or partially straight in the second configuration. Upon hydration (inside the body), the hydrophilic polymer loses its mechanical strength and allows the coated material in the catheter to return to its initial formed shape, the first configuration. Moreover, since the catheter will be prestressed through its deformation into the first configuration, greater coil retention force may be possible.

Example 8. Preparation of a Nonexpanding Interpenetrating Network Shape Memory Stent

Another example includes a biliary stent prepared using an interpenetrating network. As will be appreciated, when an interpenetrating network is utilized in a device, such as a stent or a catheter, the hydrophilic component acts to cause the device to expand. In the case of a tubular device, such as a stent or a catheter, expansion may occur both radially and longitudinally. Longitudinal expansion is sometimes not desirable.

Therefore, in order reduce or eliminate longitudinal expansion (or to attain zero length swell), the tube including the interpenetrating network is heated to a temperature above the melting point of the hydrophilic component, but below the relative transition temperature of the non-hydrophilic compound and stretched to a particular new length. The new length is chosen based upon expected longitudinal expansion of the interpenetrating network upon hydration and cooled at this new length.

The hydrophilic component, then, will act to hold the non-hydrophilic component at this new length. Upon hydration, the hydrophilic component loses its ability to hold the non-hydrophilic component in this stressed position, and the non-hydrophilic component would tend to snap back in length. However, concurrently the hydrophilic component is not only losing its ability to hold the other component, but it is expanding and beginning to hold the other component

in this stretched position by means of its expansion force. This balance of softening/shrinking versus swelling/stretching is balanced for an effective length change that is negligible.

Therefore, the use of prestretching acts to counteract longitudinal expansion of the interpenetrating network.

Example 9. Preparation of a Nonexpanding Interpenetrating Network Shape Memory Nephrostomy Catheter

A nephrostomy catheter formed from an interpenetrating network may be prepared to maintain zero length swell using the same technique as that used for the biliary stent in Example 8. The nephrostomy catheter would be held with the hydrophilic material in a prestretched position. Upon hydration the hydrophilic material would lose its ability to hold the non-hydrophilic component to allow for the accommodating length swell during hydration.

Example 10. Preparation of a Nonexpanding Interpenetrating Network Shape Memory Nephrostomy Catheter

Another example includes a nephrostomy catheter formed from an interpenetrating network which includes a hydrophilic component and a non-hydrophilic component. The nephrostomy catheter is shaped with a coil on one end through heating the catheter to a forming temperature above the relative transition temperature of the non-hydrophilic component and above the melting point of the hydrophilic component and then cooled in that configuration, the first configuration. The nephrostomy catheter is then straightened for ease of insertion on a rod and raised to a temperature above the melting point of the hydrophilic component, but below the relative transition temperature of the non-hydrophilic component and cooled in that configuration, the second configuration.

Upon hydration, the nephrostomy catheter will return to its initial shape (the first configuration), since the hydrophilic component becomes soft and flexible and loses its mechanical strength and ability to hold the non-hydrophilic

component straight in the second configuration.

Example 11. Thermally Triggered Shape Memory Devices

Devices, such as ureteral stents, which have retention mechanisms such as pigtails, coils, multicoils, etc., usually must have the retention means straightened in order for the stent to be placed onto a guide wire that is already in the body. For example, often, pigtails, as described above, are used as retention means. A physician is faced with a couple of choices. Either he or she doctor must manually straighten the retention means out, which can be difficult to do when the stent material is stiff, or certain straighteners can be used. In the case of pigtails, certain devices are pre-packaged with coaxial "pigtail straighteners" which is a tube that is stiffer than the stent material and is advanced by the surgeon over the "Pigtail" to straighten the "Pigtail" and allow a guide wire to be placed inside the straight pigtail. The Pigtail straightener is then slid to the other end and the guide wire is further advanced into the other Pigtail. This pigtail straightener is then thrown away.

In order to avoid these difficulties, however, a stent can be formed from a two component tube (i.e., an interpenetrating network, described above, or from coaxial layers). The bulk of the device would be made of a material with sufficient strength to act as a functional ureteral stent (Pellethane or Tecoflex). The balance of the device would be made of a thermally sensitive material that would lose its strength and/or change shape at body temperature.

A device can be manufactured in this manner and formed into a first conformation. For example, a ureteral stent having pigtails. The stent is then straightened to provide the second conformation. The thermally sensitive material would hold the other polymer straight to allow a straight stent to be passed over the guide wire. Once over the wire and in place in the body and at body temperature, the thermally sensitive material would allow the pigtails to form.

Methods and apparatus in accordance with the present invention, as

demonstrated above, have broad applicability in the medical device field. One area of immediate application, as mentioned above, is in the field of urology. The following discussion and embodiments are provided to illustrate the utility of the invention in the field of urology. From this discussion, it will be evident to those in the medical device arts how the particular technologies illustrated can be tailered to a variety of applications.

Figures 1A-1C illustrate one embodiment of a ureteral stent 10 in accordance with the present invention. The stent 10 comprises a tubular elongated member 12 having a selected initial cross ureteral stent outer diameter d. The elongated member 12 has a proximal end portion 16 and a distal end portion 14 joined together by a body portion 18. The proximal end portion 16 includes proximal retention means 24 for retaining the proximal end portion 16 in the kidney 28. The distal end portion 14 includes distal retention means 20 for retaining the distal end portion 14 in the bladder 22. The member 12 is formulated of a physiologically acceptable polymer that is capable of expanding to a predetermined degree. Upon insertion of the stent 10 into the ureter 30, as will be seen, referring to Figure 1B and section b of Figure 1C, the elongated member 12 hydrates and expands to form a predetermined final cross-ureteral stent outer diameter D which is selected to provide enhanced fluid passage from the kidney 28 to the bladder 22. The length of the stent 10 also generally increases upon hydration whereby the medical practitioner would start with a stent 10 somewhat shorter than that desired in the hydrated state.

A lumen 32 extends through the entire length of the stent 10 with an opening at the distal retention means 20 and a corresponding opening at the proximal retention means 24. Additionally, drainage holes 34 can cover a portion or all of the length of the stent 10. In this embodiment the fluid passage can occur through the lumen 32, the drainage holes 34 and between the wall of the ureter 30 and the exterior of the elongated member 12.

The proximal retention means 24 of this embodiment (shown here in a loop shape) comprises the proximal end portion 16 and lies in the same axial

plane as does the tubular member 12. The loop shaped distal retention means 20 comprises the distal end portion 14 of the tubular member 12 and lies in the same axial plane as does the tubular member 12. The distal retention means 20 and the proximal retention means 24 may lie within the same axial plane, or may be offset if desired. The loop shaped distal retention means 20 and proximal retention means 24 may also curl in opposite directions if desired. Although the distal retention means 20 and the proximal retention means 24 are shown in a loop shape, they can, for example, be in any desired shape which will provide adequate anchoring; each may independently be selected, for example, from hook, J-curl, helical curl, pigtail, malecot or other shapes. One very suitable shape for the distal retention means 20 and for the proximal retention means 24 is a coil with a 450° (one and one quarter) turn as shown in Figure 5. Instead of 450° the coil can have any desired amount of turning, e.g., a 540° (one and one half) turn.

The stent 10 has an initial cross-ureteral stent outer diameter d, as shown in section a of Figure 1C, which can suitably fall within a range between about 4.5 French and about 7.0 French for ease of insertion. The distal retention means 20 and the proximal retention means 24, both of which are flexible, have an initial curl diameter which is substantially larger than the initial cross-ureteral stent outer diameter d of the tubular member 12.

Similar to the discussions above, related to selection of materials for manufacture of devices in accordance with the invention, the stent 10 is preferably formulated from a physiologically acceptable polymer that is capable of softening to a predetermined degree and expanding, from generally in within forty five (45) minutes to a few hours after insertion into the ureter 30, to form a predetermined final cross-ureteral stent outer diameter D selected to provide patient comfort and to enhance fluid passage from the kidney 28 to the bladder 22. The polymer comprises a hydrophilic component capable of hydrating and expanding the selected initial cross-ureteral diameter, for example, from about five percent (5%) to about three hundred percent (300%). The stent 10 can, for

ease of insertion, initially be even stiffer than the stiff stents of the past (usually 100 Shore A to 70 Shore D) since it does not remain hard to cause discomfort to the patient once hydration has occurred.

The hydrophilic component utilized in the manufacture of the stent 10 is selected as discussed extensively above. As also discussed above, the stent 10 preferably comprises a hydrophilic component and a non-hydrophilic component in a selected ratio. The ratio of hydrophilic component to non-hydrophilic component is preferably adjustable so as to allow the polymer to expand the initial cross ureteral stent outer diameter d to a desired extent, for example, by from about five percent (5%) up to about three hundred percent (300%) upon hydration.

The polymer can be formulated so that upon hydration one portion of the stent 10, for example, the distal retention means 20, softens to a greater degree than does another portion of the stent 10, for example, the proximal retention means 24. To achieve this dual hardness after hydration, initially the ureteral stent 10 can be processed differently at the proximal end portion 16 than at the distal end portion 14. For example, the proximal retention means 24 can be cross-linked more than is the distal retention means 20, e.g., by exposing it to more polymerization initiating radiation.

The proximal retention means 24 of ureteral stent 10 can be exposed to a larger dose of electron beam cross-linking radiation whereas the distal retention means 20 can be exposed to a smaller dose, for example, by shielding it. The larger dose of electron beam cross-linking radiation yields a relatively stiffer proximal retention means 24 which softens to a lesser degree than does the distal retention means 20 upon hydration. Consequently, retention strength by the proximal retention means 24 within the kidney 28 is increased. The smaller dose of electron beam cross-linking radiation yields a relatively softer distal retention means 20 and allows it to soften to a greater degree than does the proximal retention means 24 upon hydration thereby providing increased patient comfort.

As another alternative, the stent 10 can be formulated of a central

cylindrical core of a physiologically acceptable polymer that is capable of softening and expanding to a predetermined degree upon hydration but that will not dissolve or biodegrade readily in the ureter. The stent 10 can further include an outer layer formulated of a physiologically acceptable polymer that is readily soluble or biodegradable in the ureter. For example, the outer layer can be a substantially non-cross-linked hydrophilic polymer. The dissolving of all or part of the outer layer then leads to a subsequent-to-insertion shrinking of the stent 10 to a desired extent, for example, to roughly its non-hydrated size, to allow it to be readily withdrawn from the patient after a desired length of time.

The expansion and softening of a non-hydrated stent 10 normally occur from within forty five (45) minutes to a few hours after its insertion into the ureter 30. The subsequent shrinking of stent 10 to its non-hydrated size or smaller usually takes from three days to three months as the soluble (or degradable -the term soluble is used herein to encompass all means by which the stent 10 shrinks) component is dissolved or degraded from the stent 10. The rate of shrinking and the final shrink size can be controlled by the volume ratio of hydrophilic component to non-hydrophilic component and/or the extent to which the hydrophilic component is cross-linked. The higher the initial volume of soluble component, the smaller the size of the stent 10 after the soluble component has dissolved. In addition, the higher the degree to which the soluble component is cross-linked, the slower the rate at which the soluble component will dissolve and thus the slower the rate at which the stent 10 will shrink.

The body portion 18 of ureteral stent 10 that comprises a hydrophilic component can be formulated such that the proximal end portion 16 expands preferably by up to about three hundred percent (300%) to form a final proximal end outer diameter. Alternatively, the body portion 18 can be formulated such that the distal end portion 14 expands preferably by up to about three hundred percent (300%) to form a final distal end outer diameter. If desired, both the proximal end portion 16 and the distal end portion 14 can be made to expand by up to three hundred percent (300%), but not necessarily to the same degree. The

final proximal or distal end outer diameter is necessary in certain situations so as to allow the sealing of any openings within the ureteral wall and/or the dilating of any constrictions at the respective end of the ureter. This expansion can be accomplished by controlling the degree of cross-linking, e.g., by controlling the relative amounts of radiation as with the proximal retention means 24 and the distal retention means 20.

The body portion 18 of stent 10 that comprises a hydrophilic component and a non-hydrophilic component can similarly be cross-linked to have its proximal end portion 16 or distal end portion 14 or both expand by up to three hundred percent (300%). However, the expansion of the proximal end portion 16 and/or distal end portion 14 can also be controlled by beginning with a non-hydrated stent 10 with substantially a constant outer diameter along its length, heating the non-hydrated stent 10 above the forming temperature of the non-hydrophilic component, which is above the melting temperature of the hydrophilic component, while in contact with a first mandril which molds it into having an enlarged diameter towards its proximal end portion 24, cooling the stent 10 to below the melting temperature of the hydrophilic component while it is still shaped by the first mandril, removing the stent from the first mandril, positioning the stent 10 on a second mandril which defines substantially an equal diameter along its entire length, heating the stent 10 to a temperature above the melting temperature of the hydrophilic component but below the forming temperature of the non-hydrophilic component, molding the stent 10 against the second mandril such that it has substantially an equal diameter along its entire length and cooling the stent 10 to a temperature below the melting temperature of the hydrophilic component while it is still shaped by the second mandril. On later insertion into the body, hydration of the hydrophilic component, which substantially reduces the strength of the shape set by the hydrophilic component, allows the shape molded against the second mandril to be lost and the stent 10 returns to the shape molded against the first mandril. A similar technique can be used to form the funnel shape retention means 214,216 of Figures 3A-3C.

The stent 10 can be formed so as to have no increase in length following insertion. This can be accomplished by having the physician partially uncoil the proximal retention means 24 and/or the distal retention means 20. If, for example, the coil initially has a 450° (one and one quarter) turn as shown in Figure 5, the proximal retention means 24 and/or the distal retention means 20 can be partially straightened, for example, 90° (one quarter turn) to provide a somewhat lengthened stent and then on hydrating after insertion the coil will curl back to the 450° turn to compensate for the length increase of the stent 10.

As with prior art stents, a suture 33, shown in Figure 1, can be attached to the distal end portion 14 of the stent 10 so as to allow it to be removed without the use of a cystoscope.

Referring to Figs. 2A and 2D (which illustrate an embodiment somewhat different than that of Figs. 1A-1C as will be explained later), one preferred method to place stent 110 in the patient is to insert a guide wire 35 into the patient up the ureter 30 with a proximal tip 36 of the guide wire 35 going into the kidney 28 and stopping. The stent 110 is then drawn over the distal end of the guide wire 35 to straighten the loop shaped proximal retention means 124 and the loop shaped distal retention means 120. Once the stent 110 is straightened over the guide wire 35 the stent 110 is pushed, using a tubular stent pusher 37, and thereby advanced over the guide wire 35 into the patient and into the ureter 30 stopping with its proximal end portion 116 in the kidney 28. The proximal end 140 of the proximal retention means 124 in Figure 2A can be tapered, so as to facilitate ease of insertion into the ureter 30. This can assist in the reduction of trauma to the tissues of the ureter 30. The tapered proximal end 140 may be formed through the application of shape memory technology described earlier such that upon hydration the tapered proximal end 140 expands to a diameter substantially similar to the final cross-ureteral stent outer diameter D of stent 110.

Stent 110 may also incorporate internal ribs 142 within the lumen 32 longitudinally along the body portion 118 as illustrated in Figure 10 so as to

reduce the chance of kinking while the stent 110 is advanced into the ureter 30. Kinking is not desirable since drainage from the kidney 28 to the bladder 22 can be inhibited.

As the stent 110 is advanced into the ureter 30 the progress of the stent 110 can be measured by using length markers 42 (Figure 2A) longitudinally imprinted on the stent 110. With the stent 110 properly positioned in the ureter 30 as shown in Figure 2A, the guide wire 35 can be removed. As the guide wire 35 is removed, the proximal retention means 124 reforms the loop shape and hydrates as illustrated in Figure 2B. The formation of the loop shape by the proximal retention means 124 in the appropriate position can be verified by fluoroscopic examination. As the guide wire 35 is further removed, the formation of the loop shape by the distal retention means 120 also takes place. The position of the distal retention means 120 can also be verified by observing a medial stripe 44 (Figure 2B) down the length of the stent 110.

Referring to Figures 6A and 6B, stent 110 may also be suitably placed within the ureter 30 utilizing a two piece stent pusher module 412 as illustrated. The pusher module 412 comprises a distal (to the user) end portion 414 joined by a generally straight handle portion 416. The handle portion 416 has an outer diameter d' similar to the initial cross ureteral stent outer diameter d of stent 110. The distal end portion 414 includes a shoulder 418 from which a generally cylindrical post 420 extends. The post 420 is the far end portion of a piston like member 421 which is in sliding fit within a bore 423 in a tubular member 425 which also forms a part of the pusher module 412. The cylindrical post 420 fits firmly within the lumen 32 of the stent 110 so as to allow positive engagement between the pusher module 412 and the stent 110. The positive engagement between the pusher module 412 and the stent 110 allows for forward and backward manipulation of the stent 110 during insertion. Once the stent 110 is correctly positioned within the ureter 30, the two piece pusher module 412 can be disengaged from the stent 110 by either pulling against the handle portion 416 or by retracting the post 420 to the position shown in Figure 6B. In the

embodiment illustrated the piston like member 421 fits within the tubular member 425. A spring 426 is compressed between a flange 428 on a proximal end portion 422 of the piston like member 421 and a facing flange 430 on the tubular member 425. A pin 432 fits through a lateral hole in the tubular member 425 and engages in a cavity in the piston like member 421. When disengagement of the pusher module 412 from the lumen 32 is desired, the user merely removes the pin 432 while holding the tubular member 425 from moving. The spring 426 then impels the post 420 out of engagement with the stent 110. Alternatively, the spring/pin mechanism can be omitted and the post 420 can be removed, while holding the pusher module 412 in place, by pulling upon it. Alternatively, the pusher module 412 can be removed once the stent 110 hydrates and expands. The expansion of the stent 110 loosens the pusher module 412 therefrom and the pusher module 412 can be easily removed thereafter. As illustrated, a longitudinal bore can be formed through the entire assembly, if desired, to allow for over the wire insertion.

Although shown as having a smooth outer surface, the cylindrical post 420 can be threaded as shown in Figure 7 so as to allow a tighter engagement between the pusher module 412 and the stent 110. Removal of the pusher module 412 then requires disengagement by unscrewing the pusher module 412 from the stent 110 or awaiting hydration. The spring arrangement of Figures 6A, 6B would not be present.

Figure 8 illustrates another suitable pusher module 512 for maneuvering the stent 110 into the ureter 30. One embodiment of the pusher module 512 comprises a push rod 513 having a distal (to the user) end portion 514 joined by a handle portion 516. The pusher module 512 also includes a sleeve 517 having a bore 519 in which the push rod 513 slidingly fits. A disengaging mechanism 518 is located about the handle portion 516 of the push rod 513. The push rod 513 extends between the distal end portion 514 and a push end 535 at a proximal end portion 537 of the handle portion 516. The bore 519 has an inner diameter d_1, at least at a distal end portion 539 thereof, which is substantially equal to the

initial outer diameter d of the stent 110 so as to allow a firm fit between the stent 110 and the distal end portion 539 of the bore 519. The disengaging mechanism 518 is encased within a proximal end portion 541 of the sleeve 517. It is in the nature of a chamber 543 in which a spring 545 is located about the push rod 513. The spring 545 normally biases the push rod 513 proximally (to the user) in the bore 519 by acting between a shoulder 547 defined by the chamber 543 and a flange 549 which extends from the push rod 513 and is located within the chamber 543. To disengage the stent 110 the user pushes the push end 535 of the push rod 513 relatively toward and further into the sleeve 517 while maintaining the sleeve 517 essentially stationary. This compresses the spring 545 and the distal end portion 514 of the push rod 513 impels the stent 110 out of the bore 519. As illustrated, a longitudinal bore can be formed through the entire assembly, if desired, to allow for over the wire insertion.

Referring to Figure 9 there is shown still another suitable pusher 612 for maneuvering the stent 110 into the ureter 30. One end of the pusher 612 is bonded at 613 to one end of the stent 110 forming an assemblage 614. The assemblage generally has the same outer diameter as the initial diameter d of the stent 110. The assemblage 614 can optionally include a suture 616, illustrated by a dashed line, extending from the stent 110 and imbedded longitudinally down the pusher 612. The pusher 612, if desired, may include a cylindrical portion 618, similar to that shown in Figures 6A and 6B, to enhance the firmness of the bonding between the stent 110 and the pusher 612. The pusher 612 is formulated of a body fluid soluble or biodegradable polymer capable of dissolving or degrading within a limited time after insertion of the assemblage 614 into the ureter 30. Once the pusher 612 is degraded, the stent 110 and the suture 616 remain within the ureter 30. The suture 616 being attached to the ureteral stent 110 extends to the outside of the patient so as to allow its removal without using a cystoscope. As illustrated, a longitudinal bore can be formed through the entire assembly, if desired, to allow for over the wire insertion.

Useful biodegradable polymers and dissolvable polymers are selected as

discussed extensively above. Dissolvable polymers are ofter preferable for use, since they can be readily formulated so as to dissolve in minutes to hours. The rate at which the polymer hydrates and degrades can be controlled by controlling the molecular weight and the amorphous nature of the pusher 612 composition to assure the integrity of the pusher 612 as it aids in advancing the stent 610 into the ureter 30.

After it is properly positioned within the ureter 30, the stent 110 as shown in Figure 2A has its proximal retention means 124 extend beyond the ureter 30 into the kidney 28. Similarly the distal retention means 120 extends beyond the ureter 30 into the bladder 22.

Confirmation that the stent 110 has been correctly positioned within the ureter 30 can also be obtained by x-ray or by fluoroscopy. If desired, a radiopaque material can be incorporated into the stent 110 or can be present as the measurement markings 44 along the length of the stent 110 so as to render the stent 110 visible during x-ray or fluoroscopic examination. The radiopaque material can suitably be selected from the group consisting of barium sulfate, bismuth subcarbonate, tantalum, tungsten, silver or mixtures thereof. The radiopaque material can be incorporated into the polymer from which the stent 10 is formed by melt mixing or, in the case of gels by dispersing into the gels prior to cross-linking them.

The body portion 118, being generally cylindrical in shape, has an initial cross-ureteral stent outer diameter d (see Figure 2C), the initial cross-ureteral stent outer diameter being the initial outer diameter of the tubular member 112. As the stent 110 hydrates, referring to Figure 2B, the body portion 118 expands radially to a final cross-ureteral outer diameter D, suitably to 6 French or more, with the precise size being selected in view of the size of the patient's ureter 30. Such expansion clears and restores the ureteral passage from the kidney 28 to the bladder 22. The body portion 118, upon hydration, also softens appropriately, for example to a hardness in the range from about 50 to about 100 Shore A. This considerably improves comfort within the patient.

The stent 110 as shown in Figures 2A-D may also incorporate drainage holes 134 throughout. Upon hydration, as the stent 110 expands, the drainage holes 134 also expand. As a result, the size of the drainage holes 134 increases. The presence of larger drainage holes 134 is desirable since the rate of drainage between the kidney 28 and the bladder 20 will increase.

Referring again to Figure 2B, the distal retention means 120 and the proximal retention means 124 may expand to selected curl diameters Dc (not necessarily equal to one another), upon hydration. However, the proximal retention means 124 does not necessarily have to expand. The selected curl diameter is substantially larger than the ureter diameter so as to prevent the stent 110 from migrating or being expelled from the ureter 30. The proximal retention means 124, possibly by being initially exposed to a greater dose of electron beam cross-linking radiation, can remain relatively stiff and soften to only a hardness which generally falls in a range from about 70 Shore A to about 70 Shore D. The distal retention means 120, being initially exposed to a lesser dose of electron beam cross-linking radiation, suitably softens to a hardness which falls in a range from about 30 to about 100 Shore A.

The stent 110 of Figures 2A-2D differs from the stent 10 in Figs. 1A-1C in that the loop shaped proximal retention means 124 and distal retention means 120 of stent 110 of Figures 2A-2D do not exist in stent 110 in its initial form. Instead, stent 110 is initially a substantially straight cylindrical tube. Upon hydration, the proximal end portion 116 of stent 110 and the distal end portion 114 of the stent 110 expand and curl to form the proximal retention means 124 and the distal retention means 120, respectively.

The formation of the proximal retention means 124 and/or the distal retention means 120 can be achieved through the shape memory technique by utilizing the thermal properties of the hydrophilic component and the non-hydrophilic component as described earlier.

As an alternate, the formation of the proximal retention means 124 and/or distal retention means 120 can be attained by using a composition having both a

hydrophilic component and a non-hydrophilic component. As discussed previously, such a composition can expand upon hydration. The higher the percentage of the hydrophilic component, other factors being equal, the more the composition expands. As a result, the degree of expansion can be controlled or tailored as desired by controlling the amount of hydrophilic component.

To form the proximal retention means 124, the proximal end portion 116 can be made such that in a cross section of the proximal end portion 116, there is substantially more hydrophilic component on one side, preferably fifty percent (50%) to ninety percent (90%) of the composition, than on the other side. The distal end portion 114 can be similarly made if desired. The higher percentage of hydrophilic component on one side is desirable so as to allow the composition on that side to expand upon hydration by from about five hundred percent (500%) to about eight hundred percent (800%) causing the proximal end portion 116 and/or the distal end portion 114 to curl and form the proximal retention means 124 and/or the distal retention means 120 respectively.

A third embodiment of the stent of the present invention is shown in Figs. 3A-3C. Similar to the stent 110 of Figures 2A-2D, the stent 210 of Figs. 3A-3C differs from stent 110 in that the coil shaped distal retention means 220 and the coil shaped proximal retention means 224 of stent 110 do not initially exist in stent 210. Instead, the proximal end portion 216 and the distal end portion 214 of stent 210 can flare outwardly as shown to a diameter larger than the initial tube outer diameter d of the body portion 218 of the stent 210. Figs. 3B-3C show that upon hydration the body portion 218 expands radially from an initial tube outer diameter d to a final tube outer diameter D. The distal end portion 214 and the proximal end portion 216 also expand in width (and can, but do not necessarily, contract in length) into the shape of a funnel which serves as the proximal retention means 224 within the kidney 28 and the distal retention means 220 within the bladder 22. The funnel shape retention means 220,224 of stent 210 also act to facilitate drainage. If desired, the stent 210 can be perforated throughout as shown in Figs. 3B and 3C to further facilitate drainage.

Alternatively, a stent 310 as illustrated in Figure 4 can have, instead of the funnel shape proximal retention means 224, an inverted tripod (or other multipod) shape proximal retention means 324. The tripod shape proximal retention means 324 has three similarly shaped pods 301 which form upon hydration. This facilitates drainage. Similarly, a tripod shape distal retention means 320 can be provided for the bladder 22.

An added attribute and advancement provided by the stents of the invention is that medicaments and/or antimineralization chemicals can be incorporated into the hydrophilic or partially hydrophilic polymers or can be deposited or otherwise provided on their surfaces. Incorporation into the polymers can be accomplished by any of a number of techniques including soaking in, surface coating, melt mixing and/or chemical grafting.

While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modification, and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice in the art to which the invention pertains and as may be applied to the essential features hereinbefore set forth, and as fall within the scope of the invention and the limits of the appended claims.

CLAIMS

That Which Is Claimed Is:

1. A polymeric medical device designed for internal use in a patient, comprising a polymer structure that would ordinarily assume a first conformation and a hydrophilic polymer coated upon at least a portion of the structure, the hydrophilic polymer being in a second conformation and having sufficient rigidity whereby the polymer structure is held in the second conformation, wherein upon hydration of the hydrophilic polymer the polymer structure assumes the first conformation.

2. The medical device of Claim 1, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

3. The medical device of Claim 1, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

4. The medical device of Claim 1, wherein the polymer structure comprises an interpenetrating network.

5. A polymeric medical device designed for internal use in a patient, comprising a polymer structure, the polymer structure comprising a first polymer material preconfigured into a first conformation and a second hydrophilic polymer material preconfigured into a second conformation, the first and second polymers having respective mechanical strengths, the mechanical strength of the second polymer material exceeding that of the first polymer material sufficiently so that the polymer structure is in the second conformation, wherein the second polymer material is adapted to lose its mechanical strength upon the occurrence of a triggering event and upon loss of the mechanical strength of the second

polymer, the device assumes the first conformation.

6. The medical device of Claim 5, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

7. The medical device of Claim 5, wherein the triggering event is an increase in temperature.

8. The medical device of Claim 6, wherein the triggering event is hydration of the second polymer material.

9. The medical device of Claim 5, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

10. The medical device of Claim 5, wherein the first polymer comprises an interpenetrating network.

11. The medical device of Claim 5, wherein the polymer structure comprises an interpenetrating network.

12. A method to manufacture a polymeric structure having shape memory properties, comprising:

providing a polymeric structure comprising a first polymer formed into a first conformation;

applying a hydrophilic polymer to at least a portion of a surface of the polymeric structure;

deforming the polymeric structure from the first conformation into a second conformation under conditions designed to permit the polymeric structure to retain a memory of the first conformation; and

allowing the hydrophilic polymer to harden and hold the polymeric structure in the second conformation.

13. The method of Claim 12, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

14. The method of Claim 12, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

15. A method to manufacture a polymeric structure having shape memory properties, comprising:

a. providing a polymeric structure comprising a first polymer and a second polymer formed into a first conformation, the first and second polymers having respective mechanical strengths, the second polymer being capable of losing its mechanical strength upon the occurrence of a triggering event; and

b. deforming the polymeric structure from the first conformation into a second conformation under conditions designed to permit the polymeric structure to retain the memory of the first conformation and to permit the mechanical strength of the second polymer to hold the polymeric structure in the second conformation.

16. The method of Claim 15, wherein the second polymer is a hydrophilic polymer.

17. The method of Claim 16, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches,

modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

18. The method of Claim 15, wherein the triggering event is an increase in temperature.

19. The method of Claim 16, wherein the triggering event is hydration of the second polymer material.

20. The method Claim 16, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

21. A medical device designed for internal use in a patient, comprising a structure that would ordinarily assume a first conformation and a hydrophilic polymer coated upon at least a portion of the structure, the hydrophilic polymer being in a second conformation and having sufficient rigidity whereby the structure is held in the second conformation, wherein upon hydration of the hydrophilic polymer the structure assumes the first conformation.

22. The medical device of Claim 21, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

23. The medical device of Claim 21, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

24. A medical device designed for internal use in a patient, comprising a structure, the structure comprising a first material preconfigured into a first conformation and a hydrophilic polymer material preconfigured into a second conformation, the first material and the hydrophilic polymer having respective mechanical strengths, the mechanical strength of the hydrophilic polymer material exceeding that of the first material sufficiently so that the structure is in the

second conformation, wherein the hydrophilic polymer material is adapted to lose its mechanical strength upon the occurrence of a triggering event and upon loss of the mechanical strength of the hydrophilic polymer, the device assumes the first conformation.

25. The medical device of Claim 24, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

26. The medical device of Claim 24, wherein the triggering event is an increase in temperature.

27. The medical device of Claim 24, wherein the triggering event is hydration of the hydrophilic polymer material.

28. The medical device of Claim 25, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

29. A method to manufacture a medical device having shape memory properties, comprising:

providing a medical device comprising a first material formed into a first conformation;

applying a hydrophilic polymer to at least a portion of a surface of the device;

deforming the device from the first conformation into a second conformation under conditions designed to permit the device to retain a memory of the first conformation; and

allowing the hydrophilic polymer to harden and hold the device in the second conformation.

30. The method of Claim 29, wherein the hydrophilic polymer is

selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and copolymers thereof.

31. The method of Claim 29, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

32. A method to manufacture a medical device having shape memory properties, comprising:

a. providing a medical device comprising a first material and a first polymer formed into a first conformation, the first material and the first polymer having respective mechanical strengths, the first polymer being capable of losing its mechanical strength upon the occurrence of a triggering event; and

b. deforming the device from the first conformation into a second conformation under conditions designed to permit the device to retain the memory of the first conformation and to permit the mechanical strength of the first polymer to hold the device in the second conformation.

33. The method of Claim 32, wherein the second polymer is a hydrophilic polymer.

34. The method of Claim 33, wherein the hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), polyvinyl pyrrolidone, polyvinyl alcohol, poly(ethylene glycol), polyacrylamide, poly (hydroxy alkyl methacrylates), poly(hydroxy ethyl methacrylate), hydrophilic polyurethanes, HYPAN, oriented HYPAN, poly(hydroxy ethyl acrylate), hydroxy ethyl cellulose, hydroxy propyl cellulose, methoxylated pectin gels, agar, starches, modified starches, alginates, hydroxy ethyl carbohydrates and mixtures and

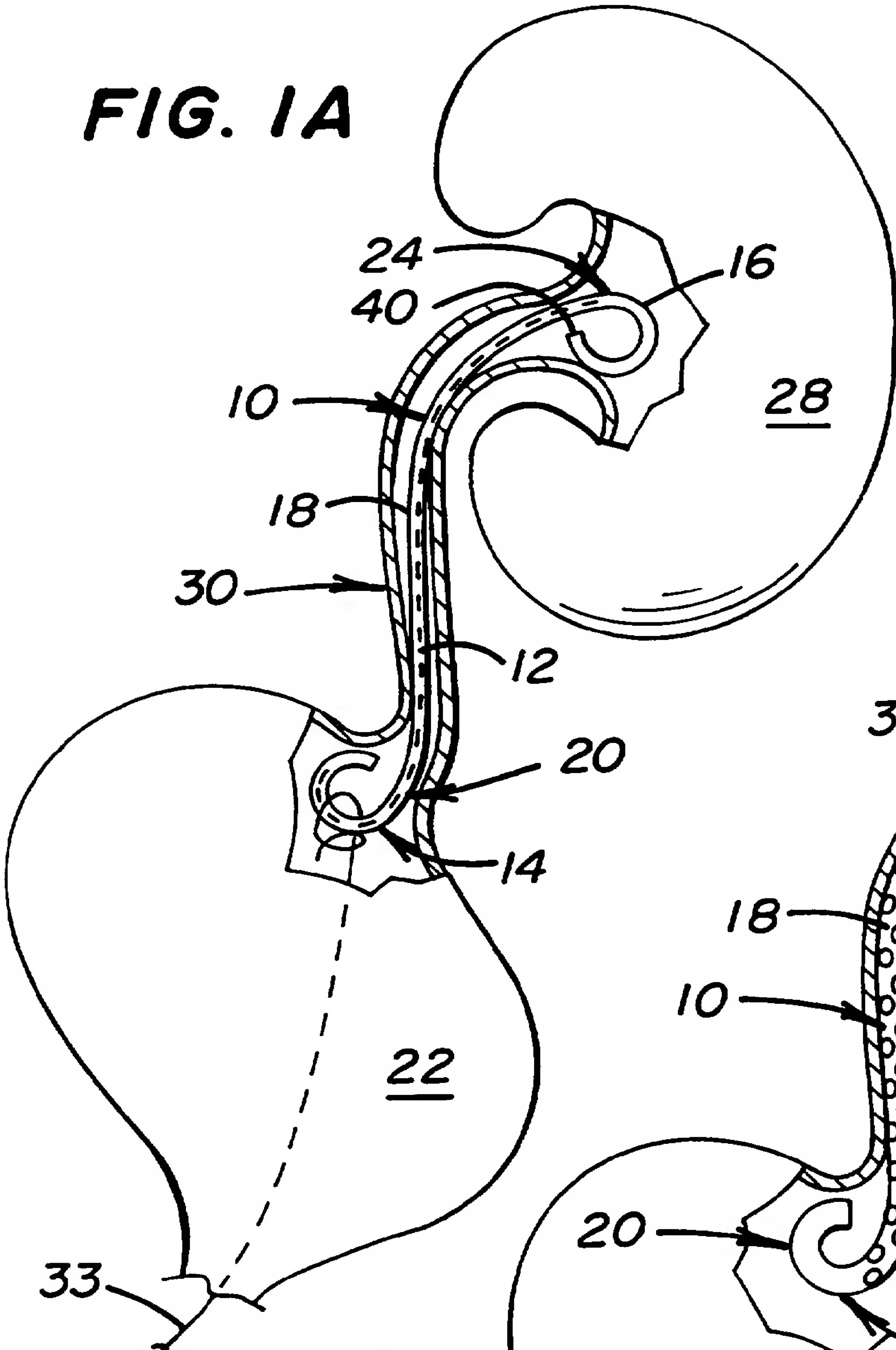
copolymers thereof.

35. The method of Claim 32, wherein the triggering event is an increase in temperature.

36. The method of Claim 33, wherein the triggering event is hydration of the second polymer material.

37. The method Claim 33, wherein the hydrophilic polymer, upon hydration, softens and expands by from about 5% to about 300%.

FIG. 1A



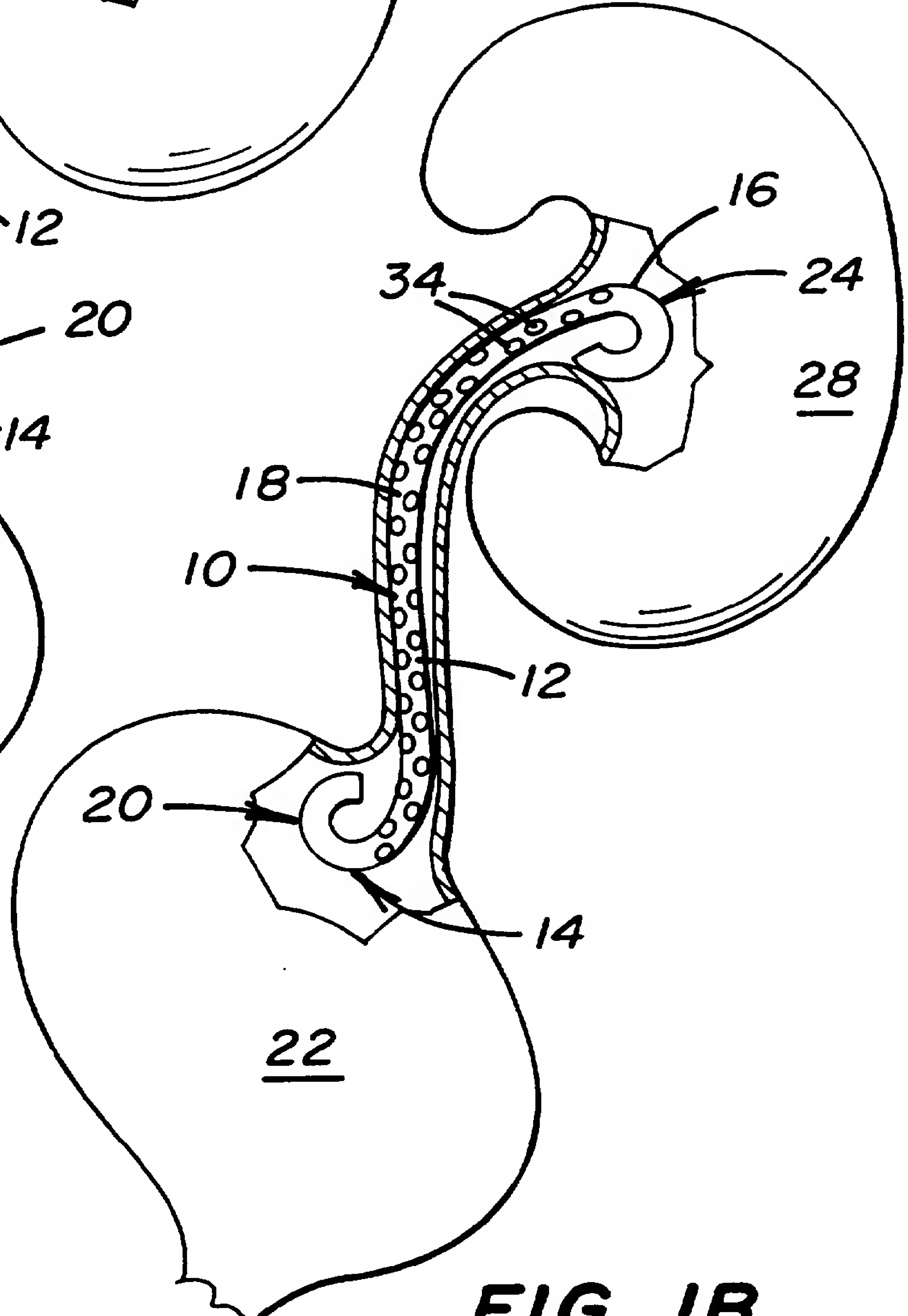


FIG. 1B

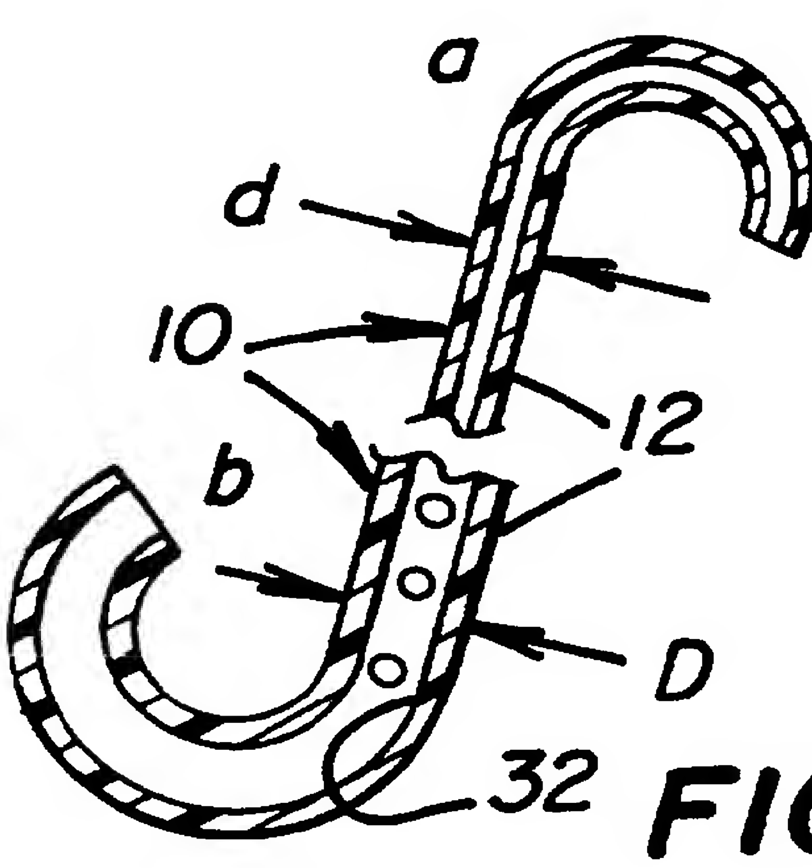


FIG. 1C

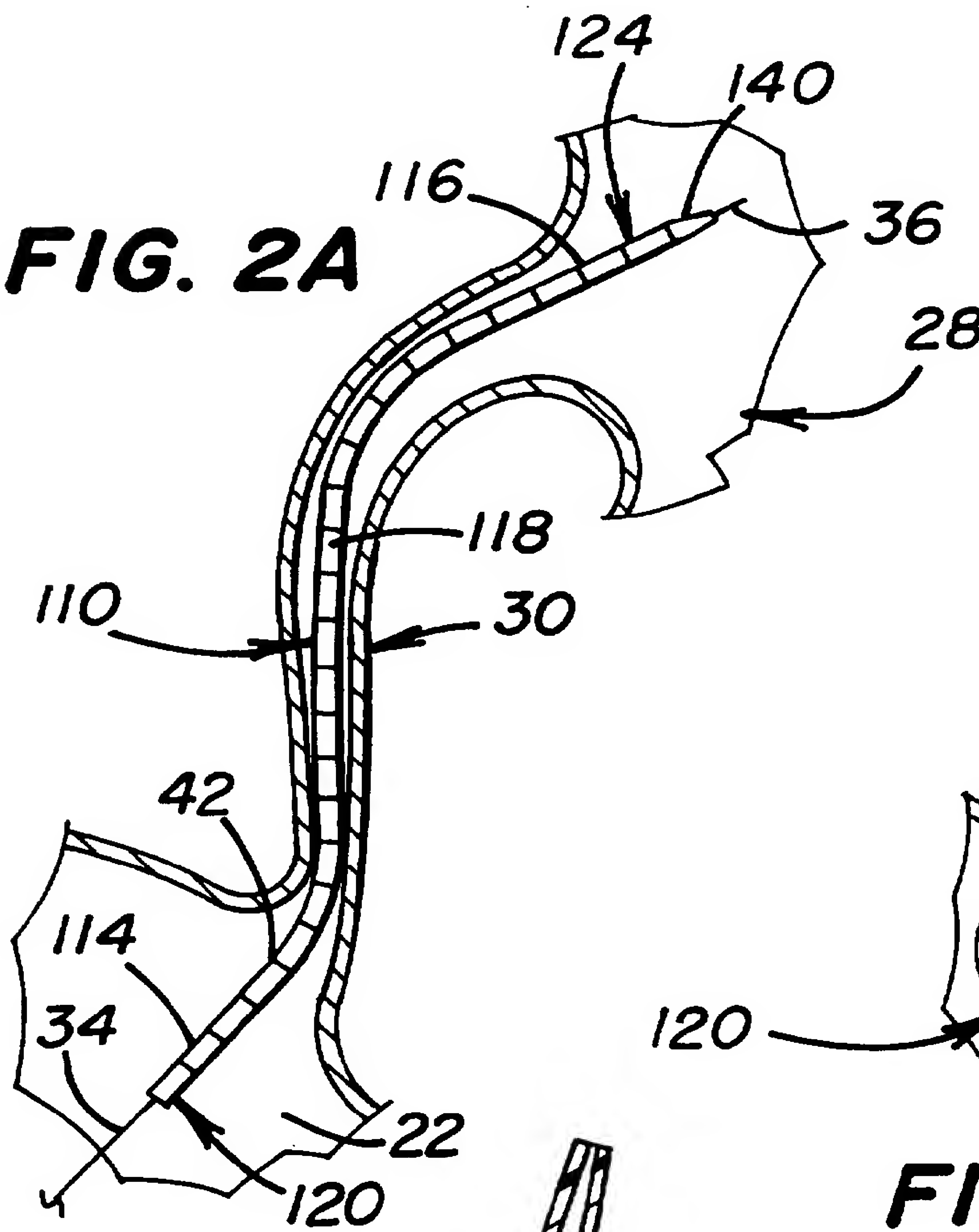


FIG. 2A

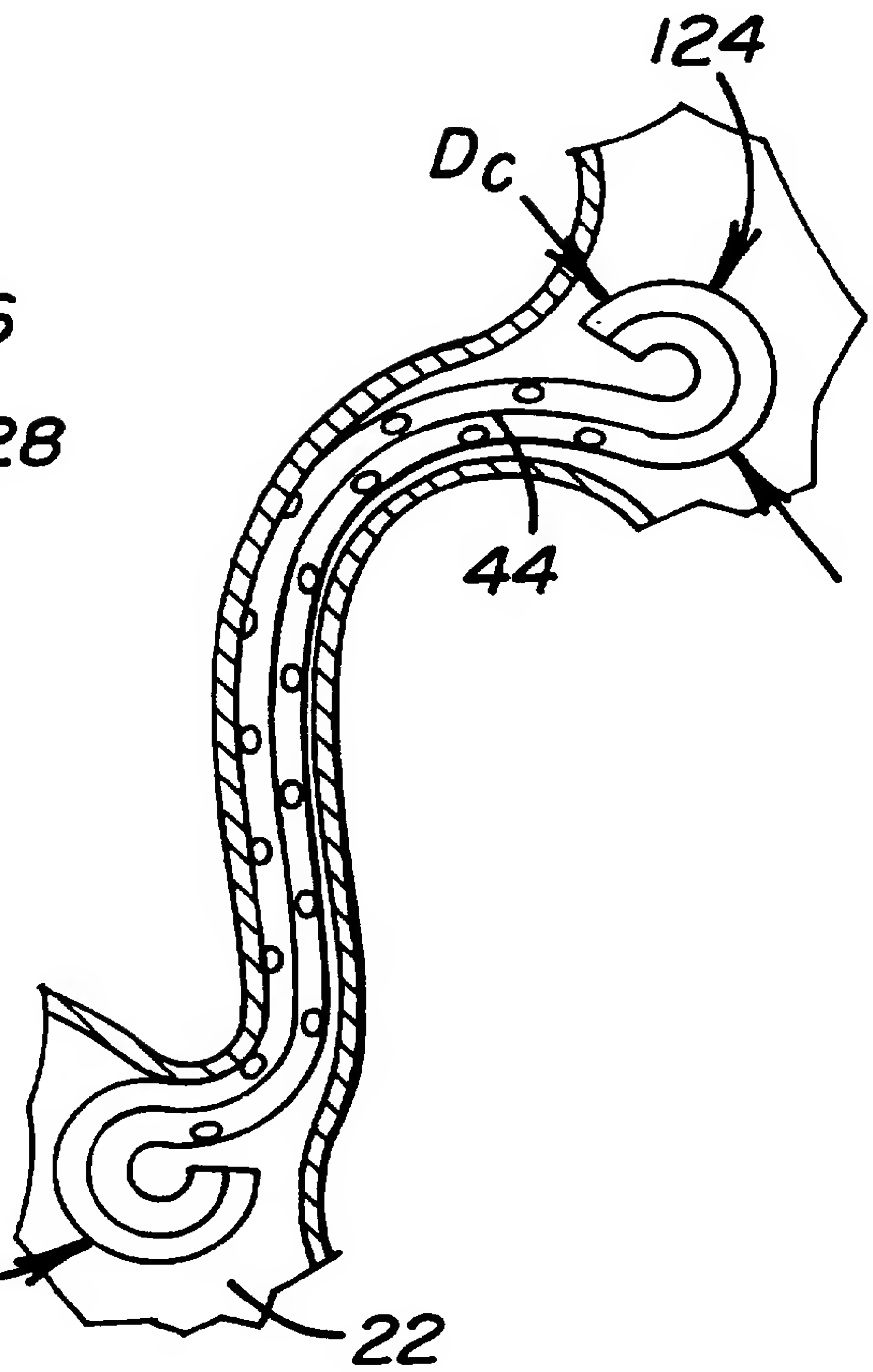


FIG. 2B

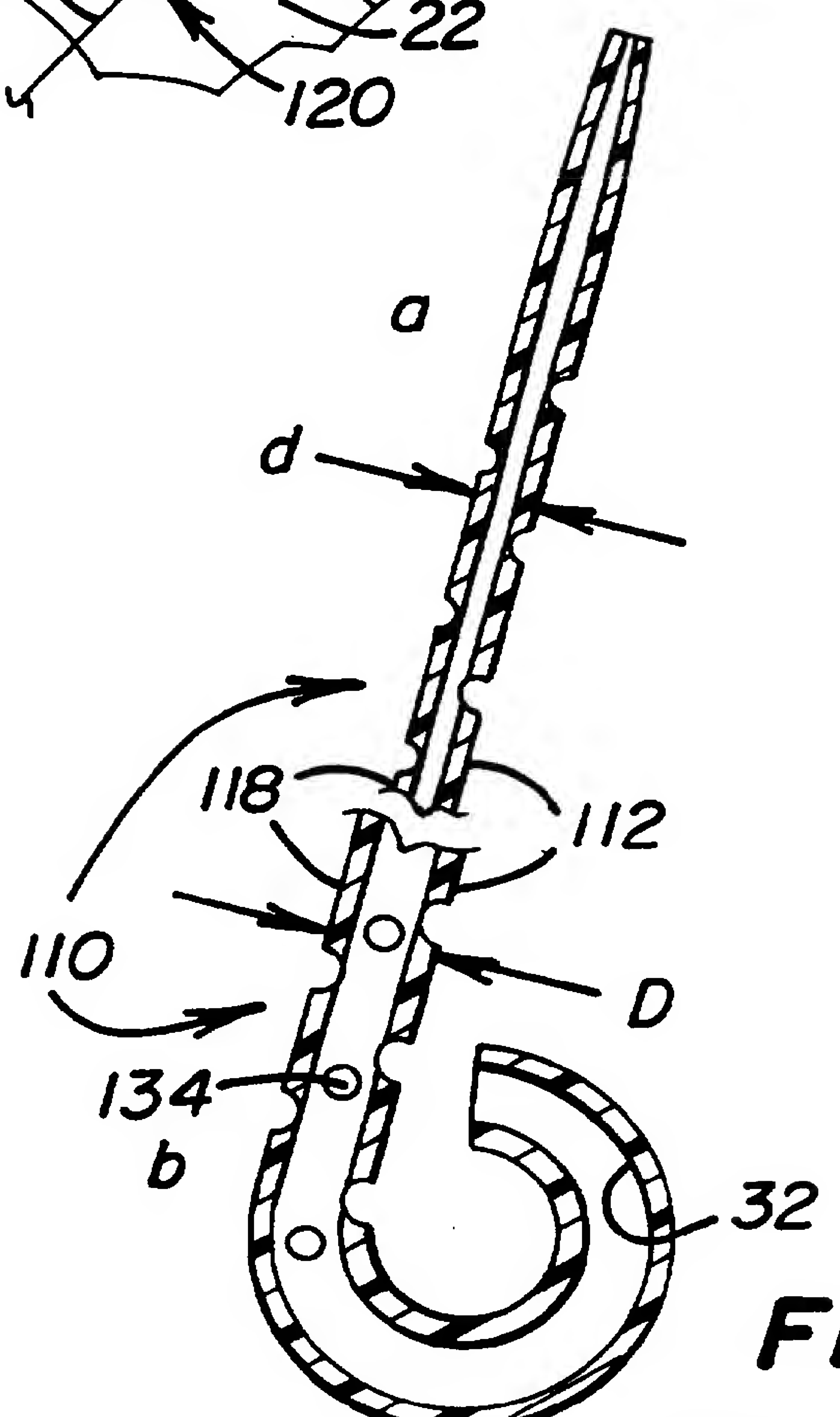


FIG. 2C

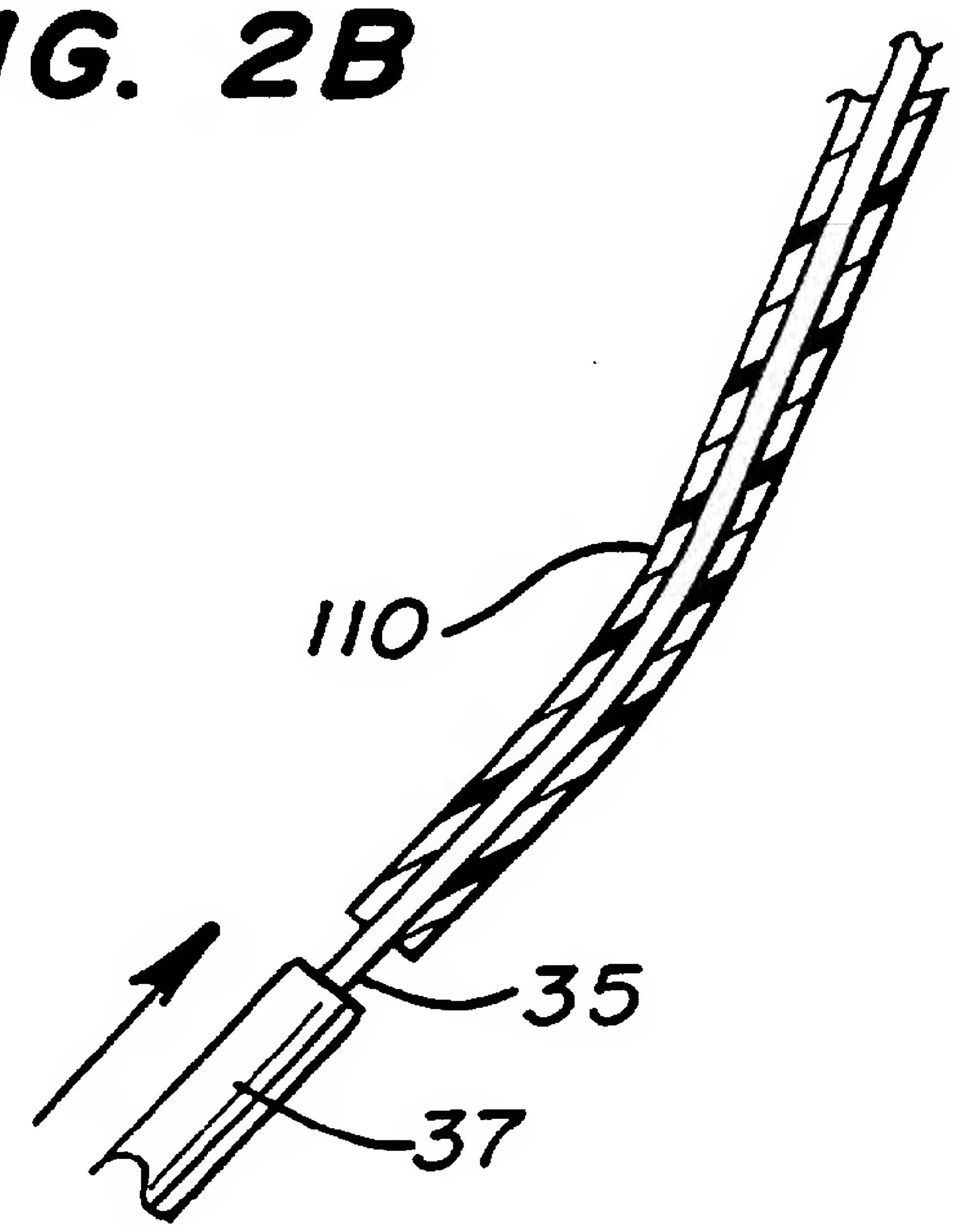


FIG. 2D

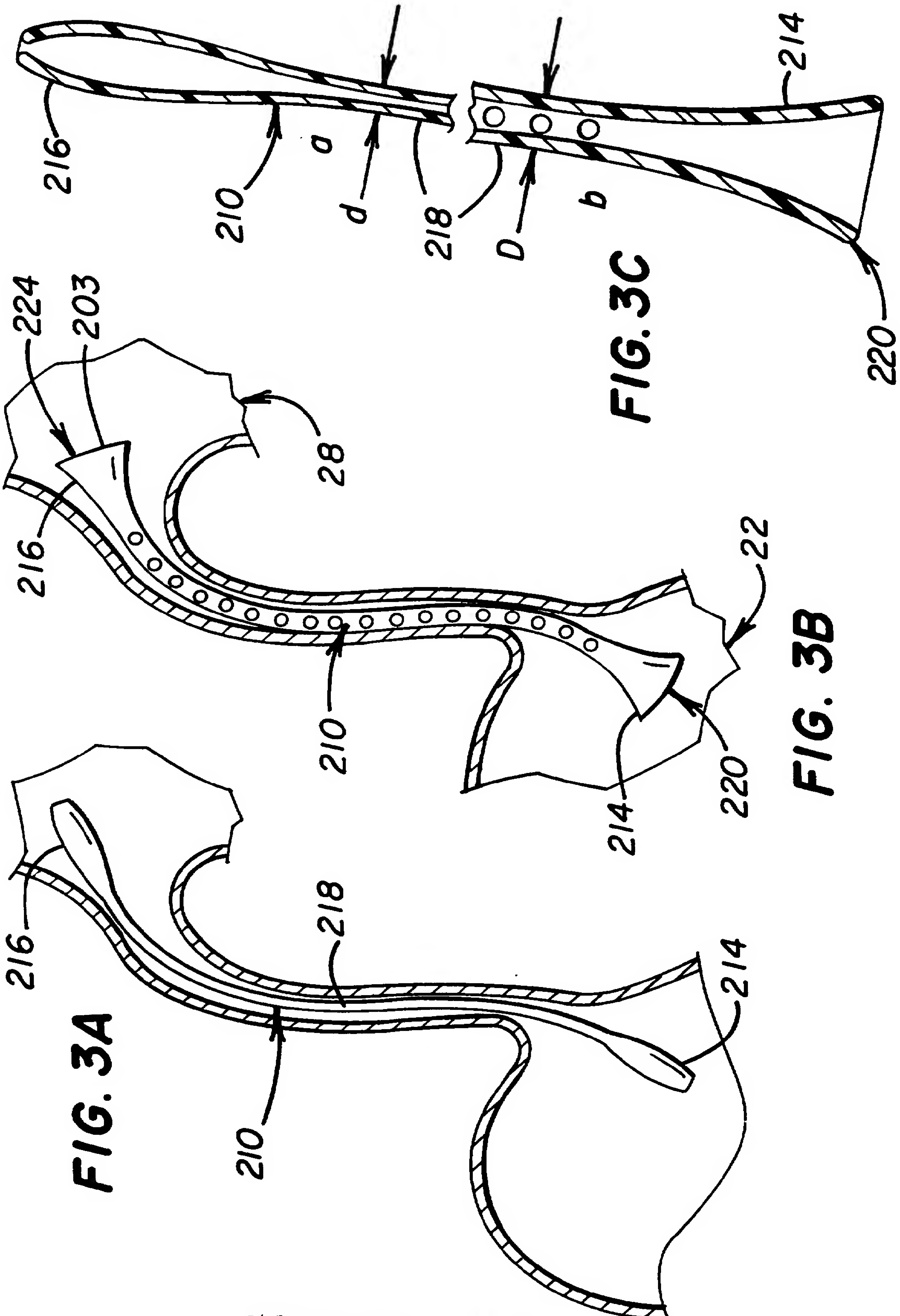


FIG. 3A

FIG. 3B

FIG. 3C

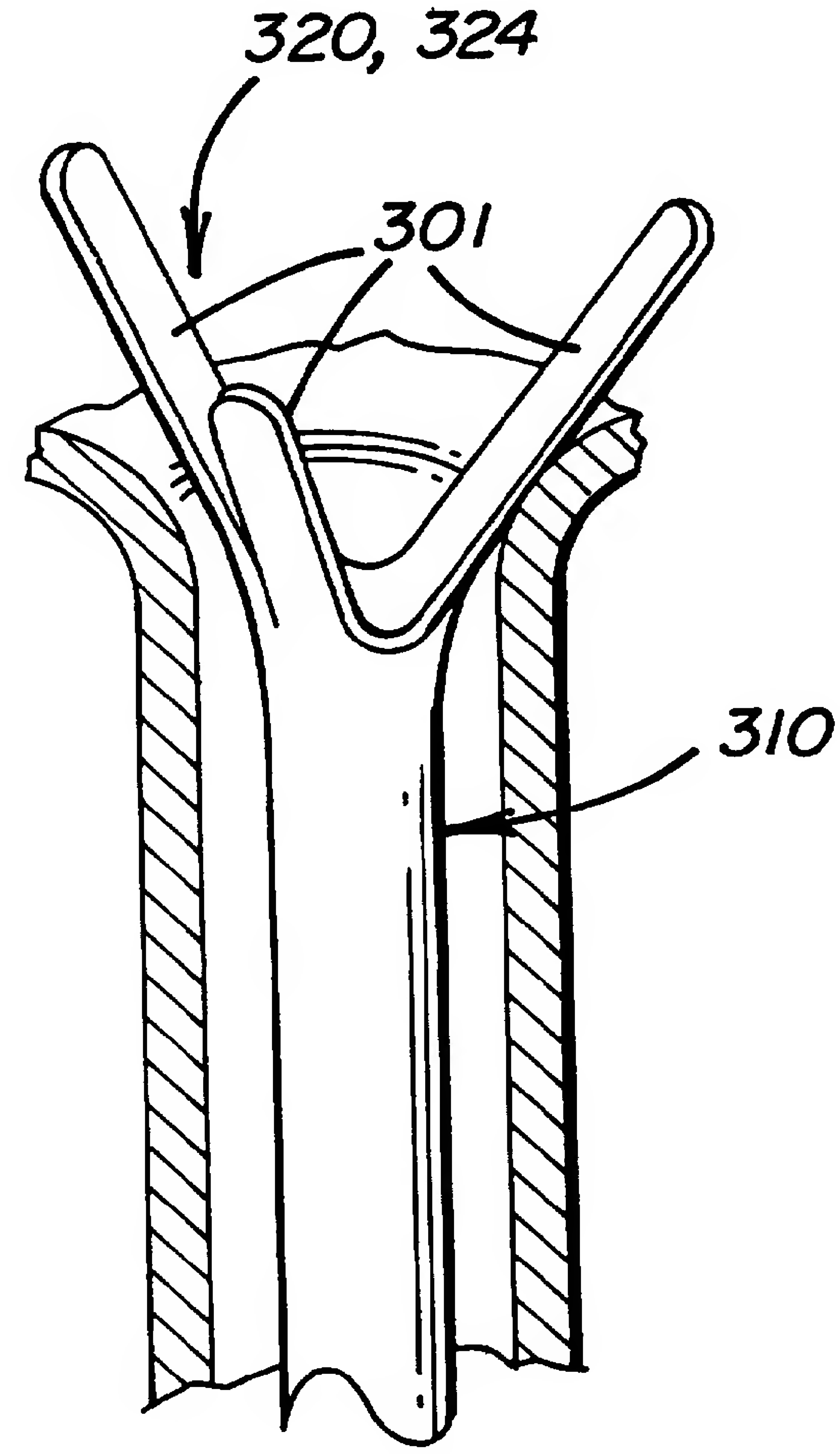


FIG. 4

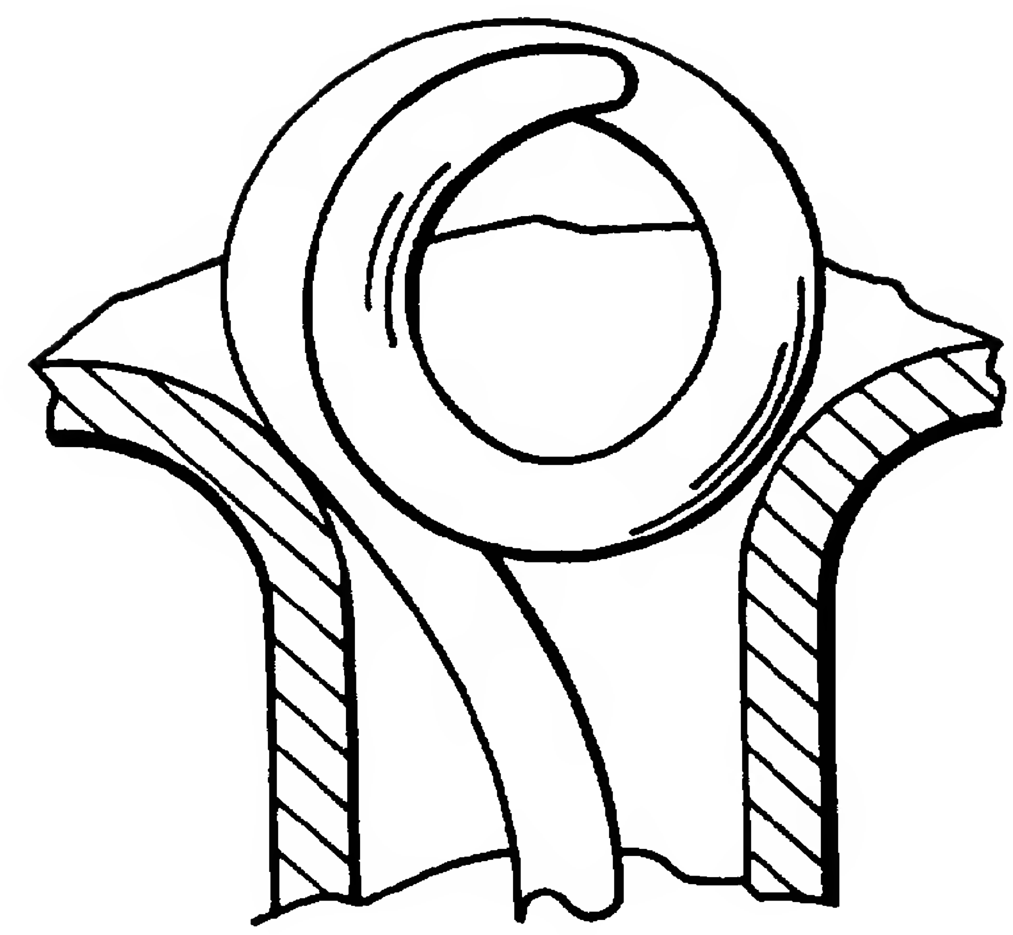


FIG. 5

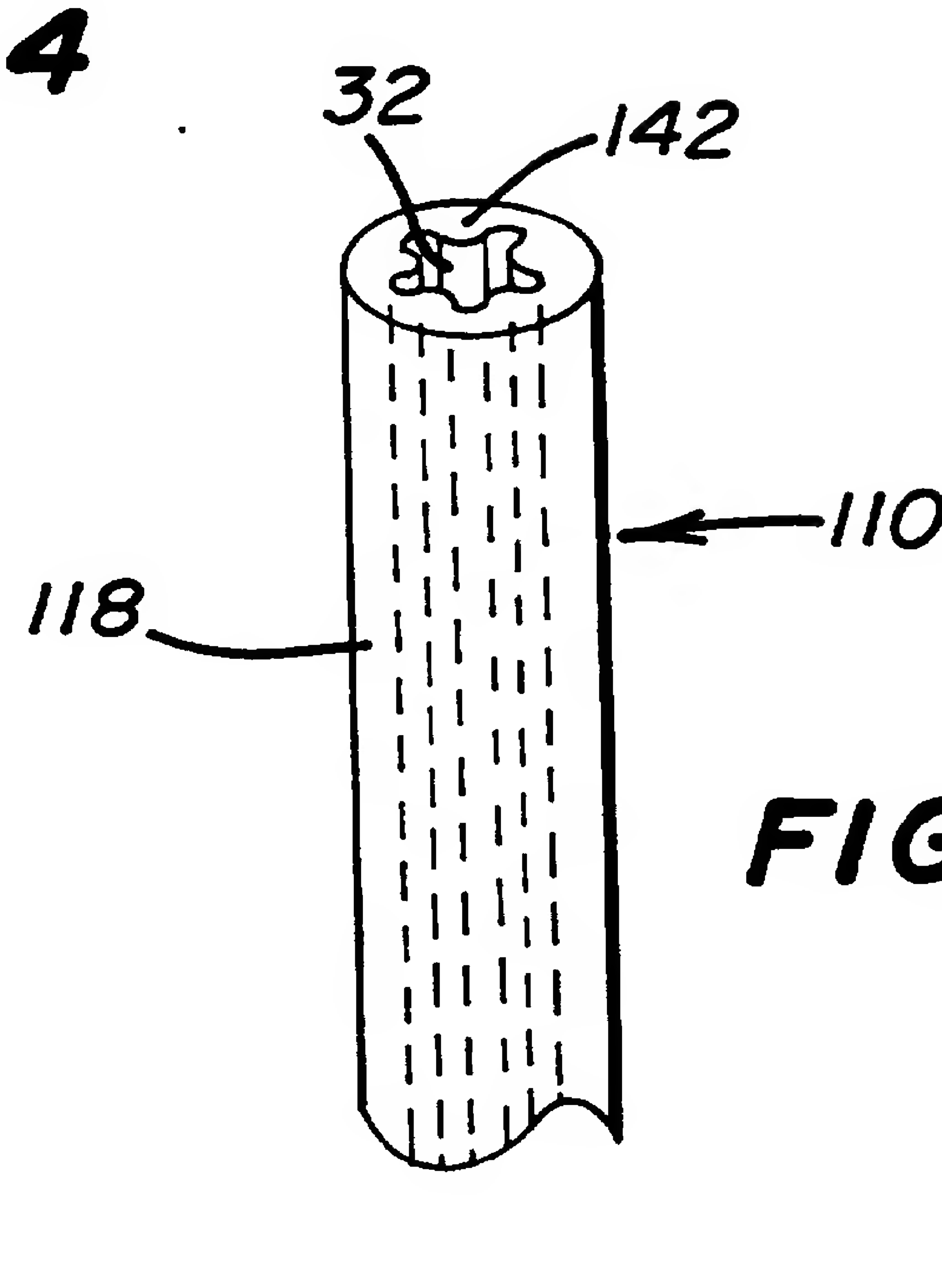


FIG. 10

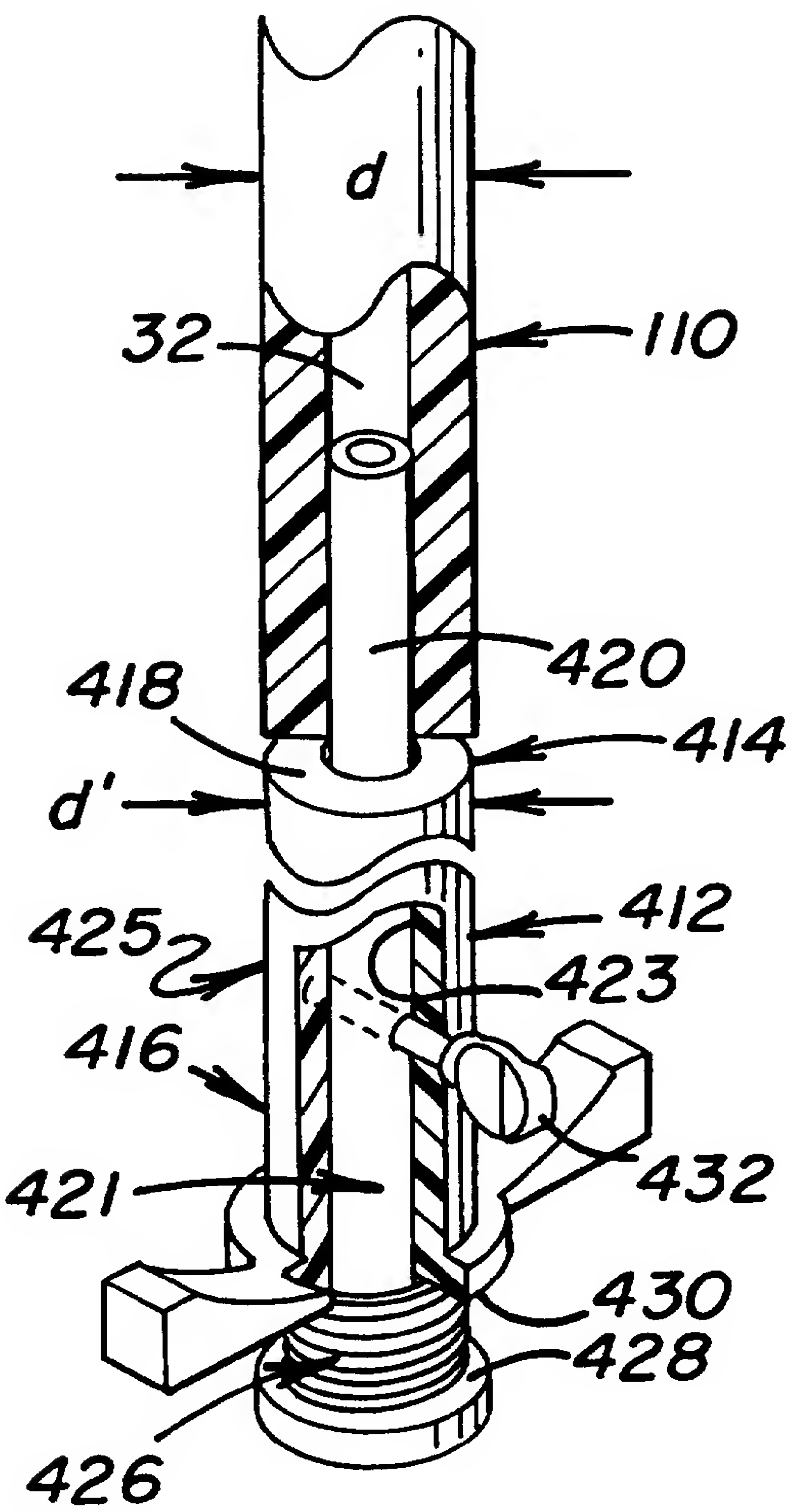


FIG. 6A

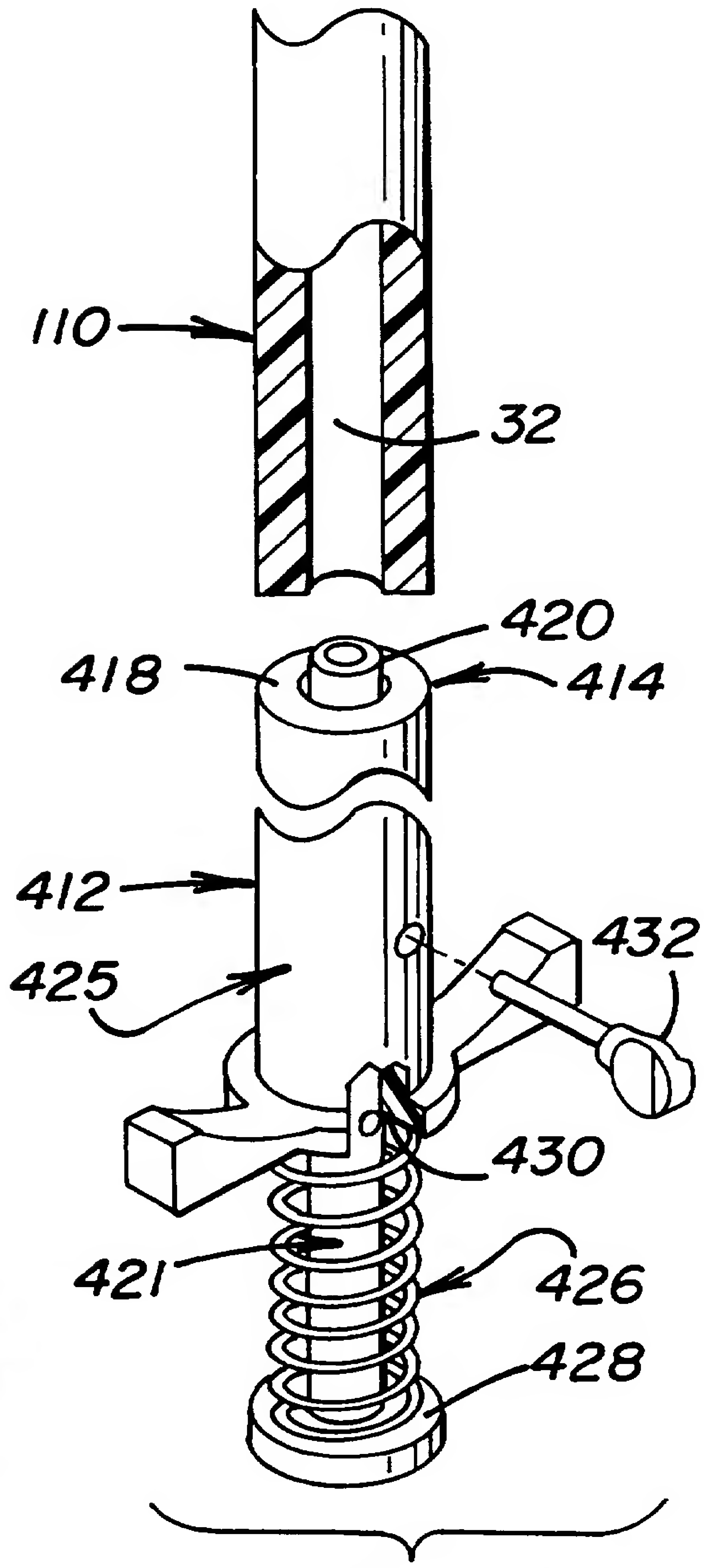


FIG. 6B

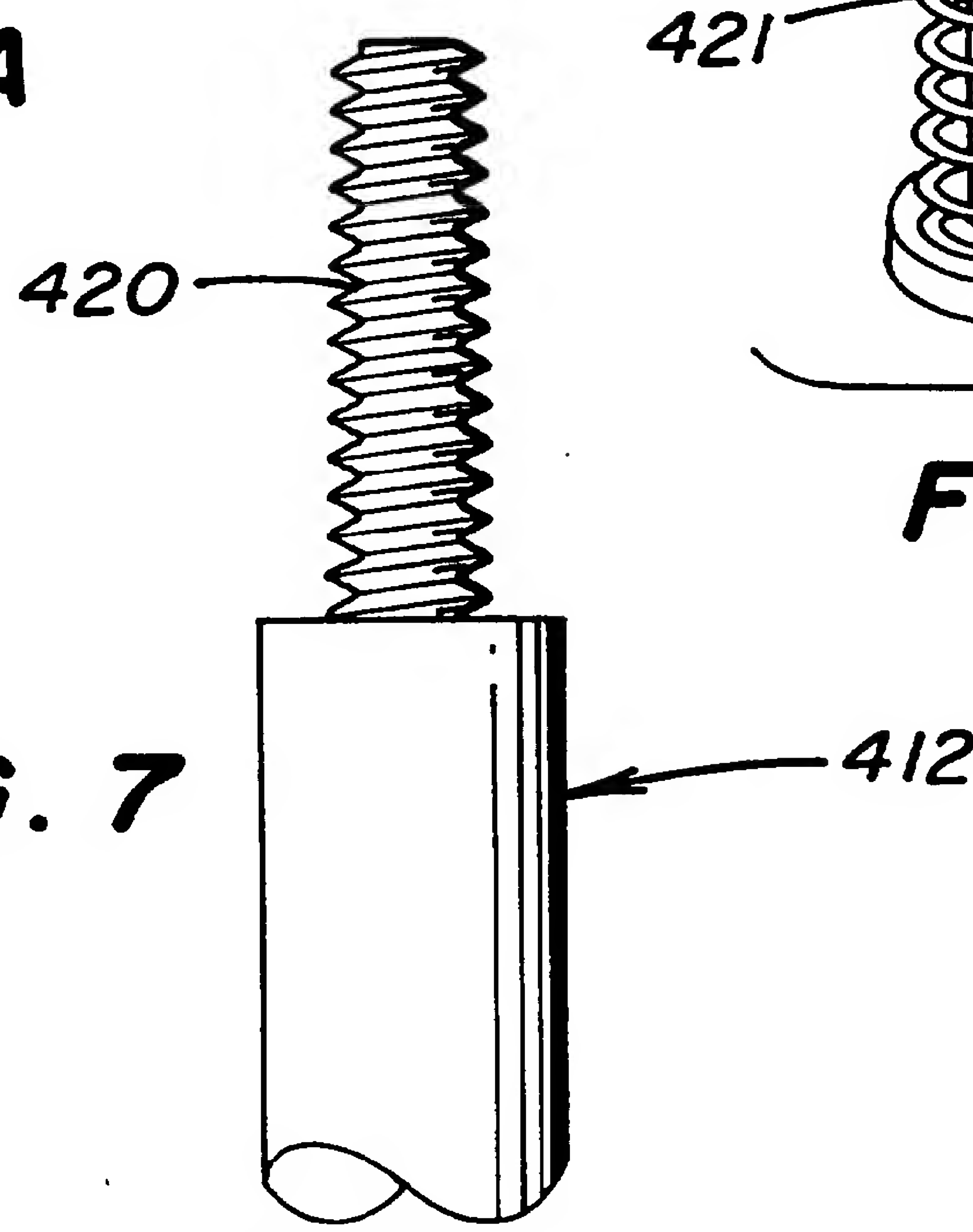
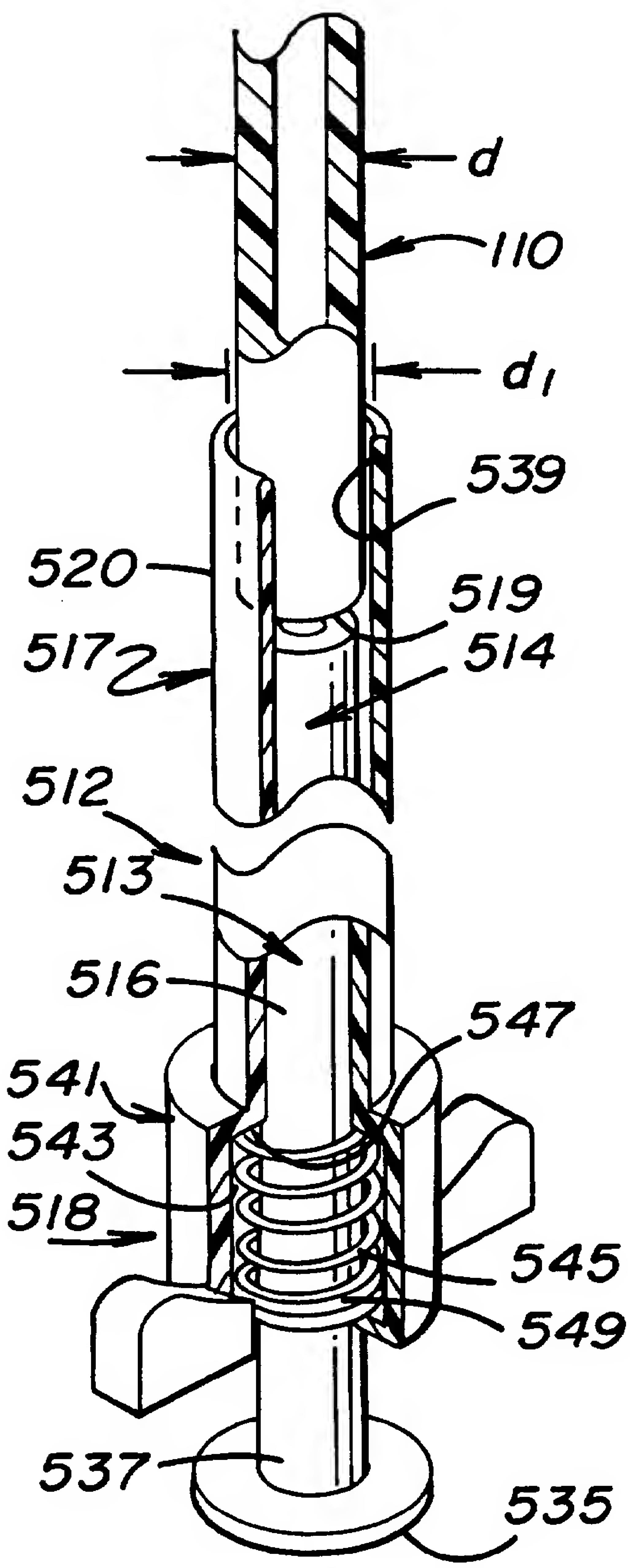


FIG. 7


d
110
d1
539
520
519
517
514
512
513
516
547
541
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537
535

FIG. 8

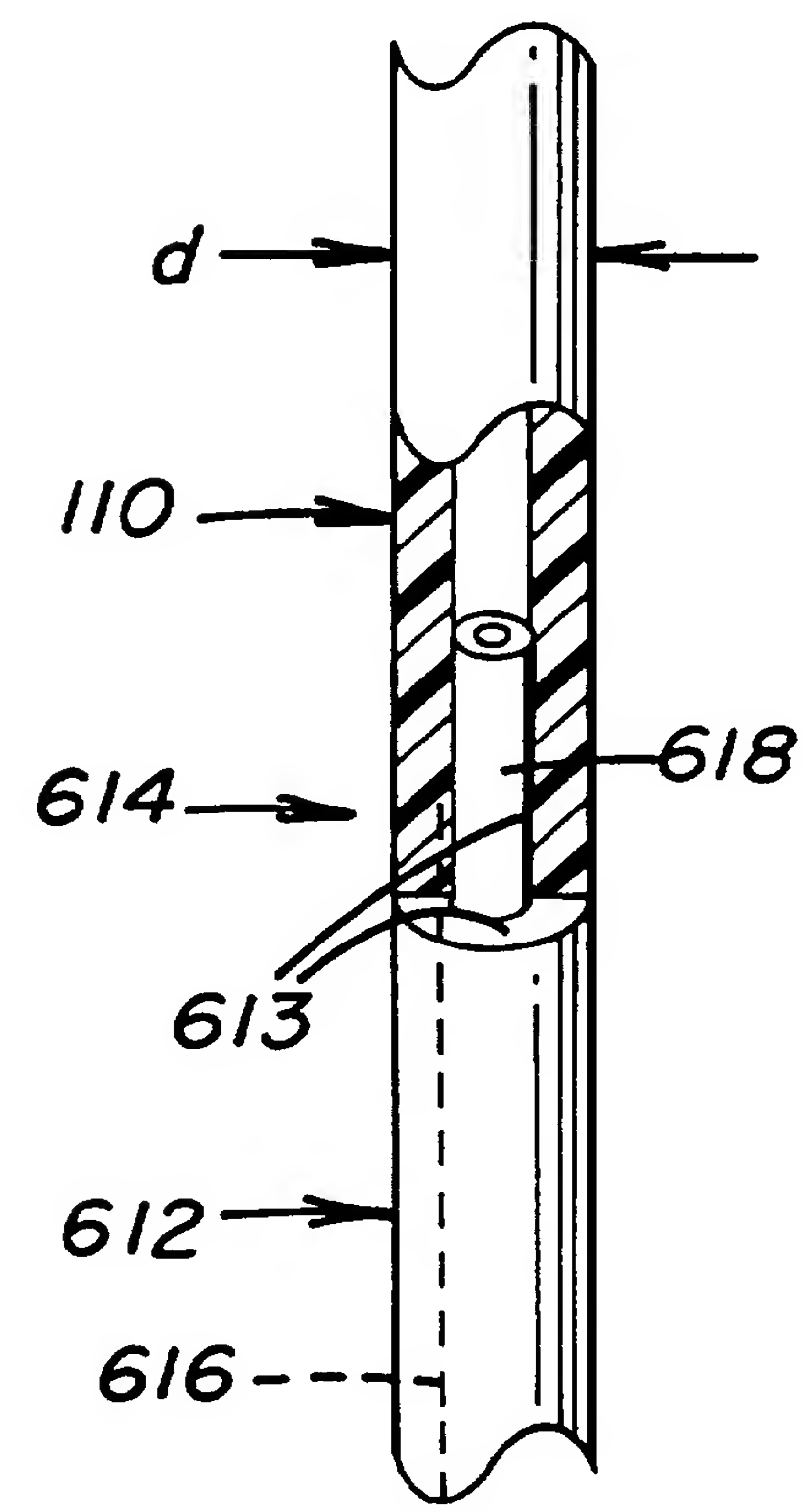
d
110
614
618
613
612
616

FIG. 9

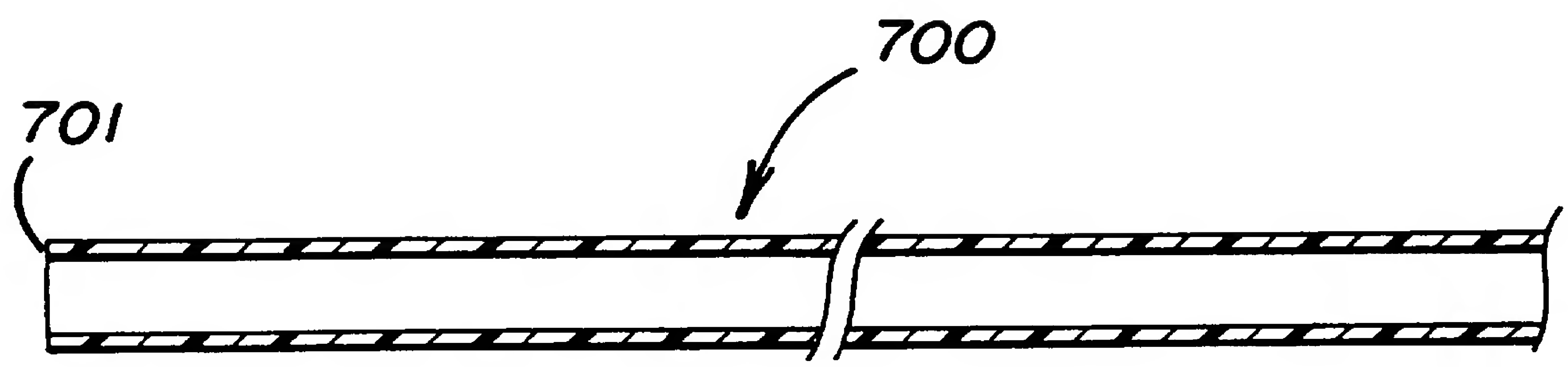

FIG. 11a

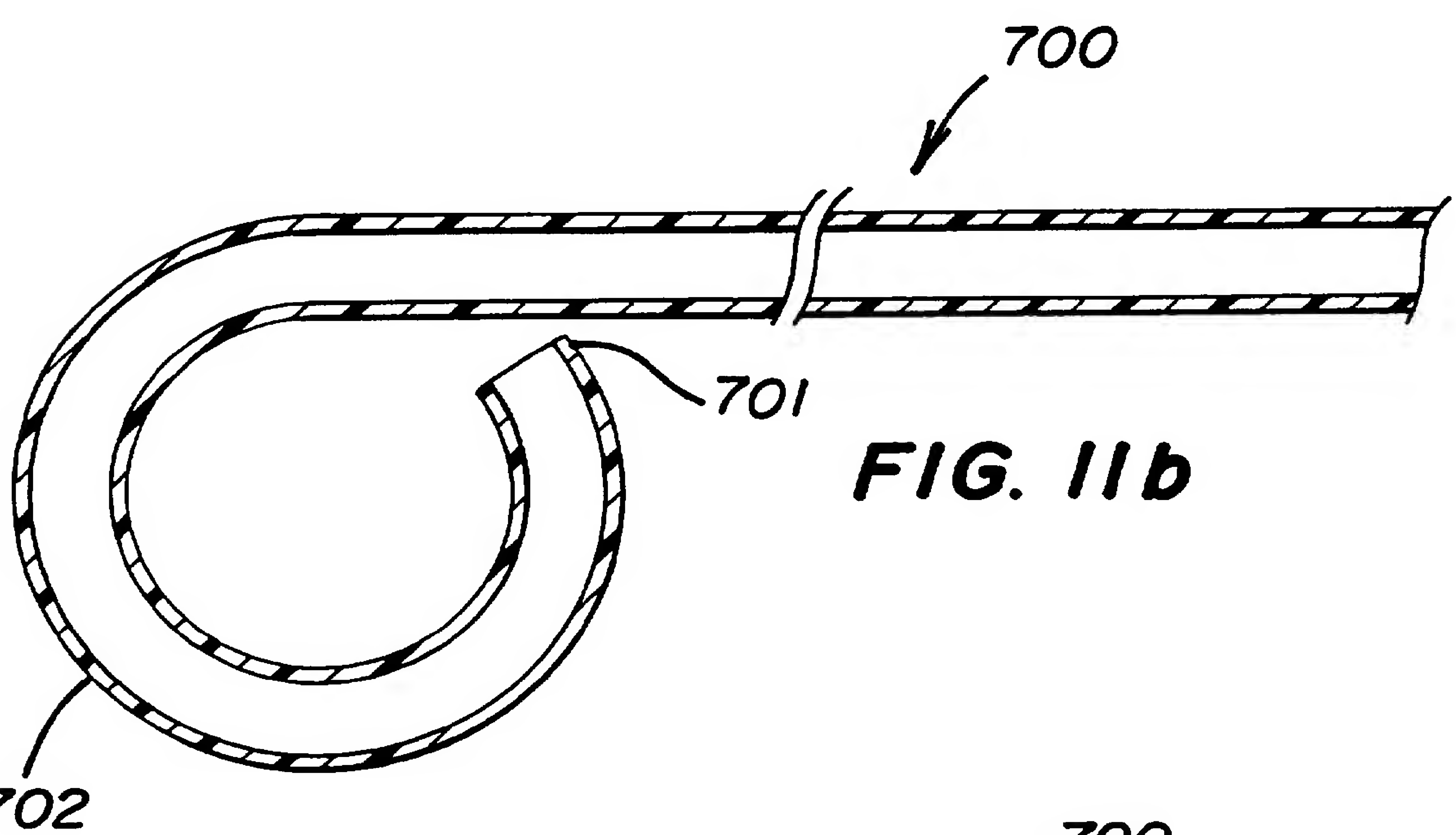

FIG. 11b

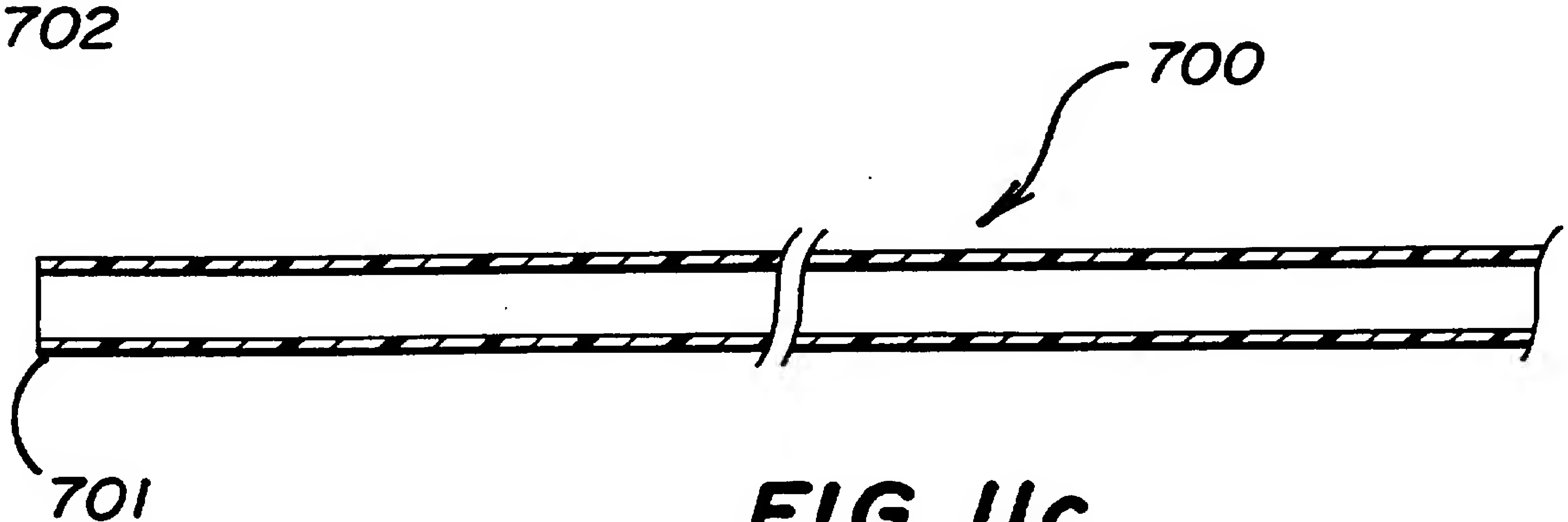

FIG. 11c

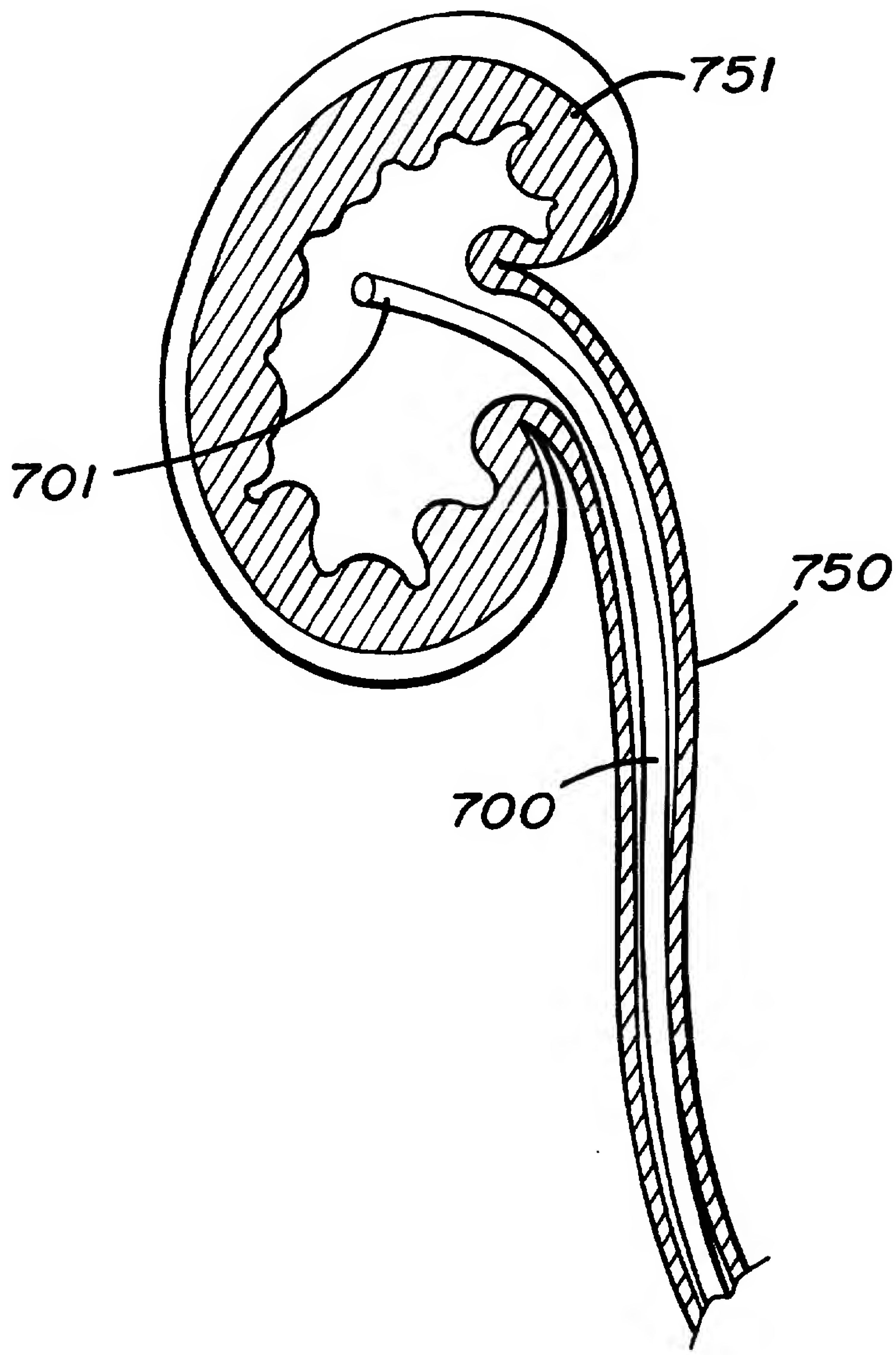

FIG. 11d

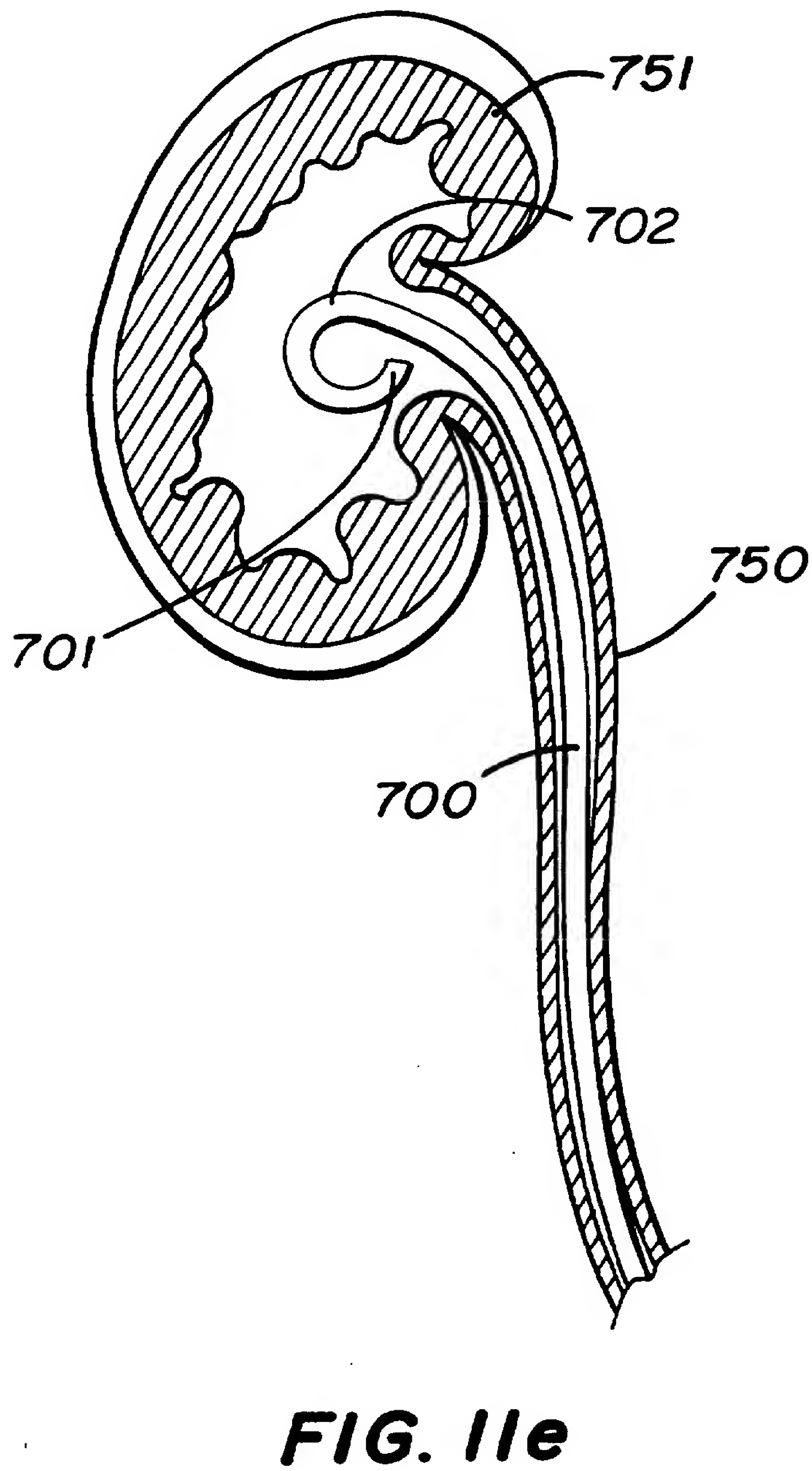

FIG. 11e

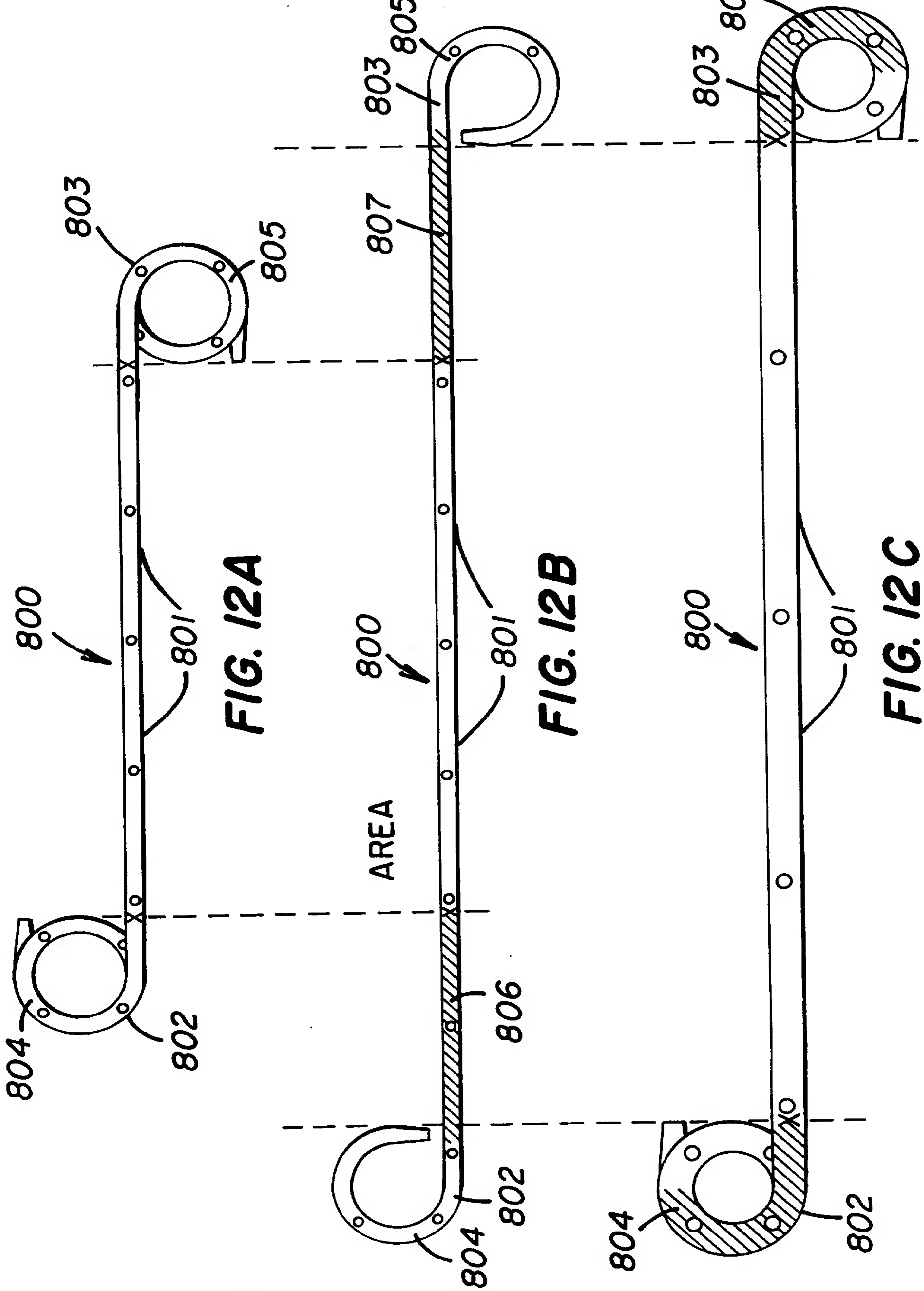

FIG. 12A

FIG. 12B

FIG. 12C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/12826

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61M 37/00
US CL :604/8
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/8-10, 175, 264, 283

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, HYDROGELS: SPECIALTY PLASTICS FOR BIOMEDICAL, PHARMACEUTICAL AND INDUSTRIAL APPLICATIONS, (STOY ET AL.), April 1990, see entire reference.	1-37
Y	US, A, KINGSTON TECHNOLOGIES, A Brief Description of the Company, Its Products and Technology, June 1989, see entire reference.	1-37

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be part of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
09 JANUARY 1996	31 JAN 1996

Name and mailing address of the ISA/US	Authorized officer
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